**Clean Energy Production Technologies**
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# Hemicellulose Biorefinery: A Sustainable Solution for Value Addition to Bio-Based Products and Bioenergy

Springer

# Clean Energy Production Technologies

**Series Editors**

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The consumption of fossil fuels has been continuously increasing around the globe and simultaneously becoming the primary cause of global warming as well as environmental pollution. Due to limited life span of fossil fuels and limited alternate energy options, energy crises is important concern faced by the world. Amidst these complex environmental and economic scenarios, renewable energy alternates such as biodiesel, hydrogen, wind, solar and bioenergy sources, which can produce energy with zero carbon residue are emerging as excellent clean energy source. For maximizing the efficiency and productivity of clean fuels via green & renewable methods, it's crucial to understand the configuration, sustainability and techno-economic feasibility of these promising energy alternates. The book series presents a comprehensive coverage combining the domains of exploring clean sources of energy and ensuring its production in an economical as well as ecologically feasible fashion. Series involves renowned experts and academicians as volume-editors and authors, from all the regions of the world. Series brings forth latest research, approaches and perspectives on clean energy production from both developed and developing parts of world under one umbrella. It is curated and developed by authoritative institutions and experts to serves global readership on this theme.

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Editor

# Hemicellulose Biorefinery: A Sustainable Solution for Value Addition to Bio-Based Products and Bioenergy

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ISSN 2662-6861 ISSN 2662-687X (electronic)
Clean Energy Production Technologies
ISBN 978-981-16-3681-3 ISBN 978-981-16-3682-0 (eBook)
https://doi.org/10.1007/978-981-16-3682-0

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# Preface

The twenty-first century has a remarkable increase in concerns related to environmental preservation, human health, food, and eco-friendly process development. In this context, the biorefinery concept has been applied for sustainable development and bioproducts for human consumption. Biomass is the raw material in the biorefinery process that through its breakdown produces macromolecules/polymers and important derivatives. Hemicellulose is a polysaccharide present in lignocellulosic materials and a precursor for different bioproducts. For example, from biomass can be produced biocomponents that are added to foods that work as prebiotic supplements, which have an increased market. Hemicellulose derivatives (including furan compounds) are key components in a platform for the production of chemicals, biofuels, plastics, and pharmaceuticals. Hemicellulose can collaborate to face the most important human challenges: energy production, sustainable feedstock source, and environmental protection. There is a prevailing need that seeks alternative energy sources, alternative biopolymers, biodegradable materials, and polymer/chemicals for advanced material production. Hemicellulose is appropriate to these applications, contributing to decrease the fossil dependence for fuels and chemicals obtaining. The use of hemicellulose in biodegradable materials contributes to reduce environmental consequences provoked by non-renewable industrial products.

This book *Hemicellulose Biorefinery: A Sustainable Solution for Value Addition to Bio-based Products and Bioenergy* is motivated by relevant contributions of hemicellulose in solving industrial processes and product challenges. Hemicellulose study can focus on its use associated with a running industrial process, or by its own valorization with a unique focus on high value-added products chain. The objective of this book is to provide an interdisciplinary view of various aspects of hemicellulose utilization in a biorefinery system. In this sense, the book can serve as an important source of knowledge (basic aspects to advanced processing and application) for students, researchers, and professors.

The hemicellulose utilization concept is aligned with new products, searching for sustainable processes. Several industrial processes waste hemicellulose as well as generate several residues rich in hemicellulose. Biorefinery has been suggested as a key aspect not only for the production of hemicellulose but as a strong contributor to whole process feasibility (Chap. 1). Moreover, combined or individual processes generating hemicellulose and its derivatives need an understanding of contributions in the circular bioeconomy (Chap. 2) and its life cycle (Chap. 3). Some chapters introduce the idea of hemicellulose solubilization/production; however, a deep understanding of its chemical composition and structure is needed (Chap. 4), as well as its chemical, physicochemical, and biological characterization (Chap. 5). Hemicellulose can have improved properties according to new perspectives of application by chemical (Chap. 6) or biological modifications (Chap. 7). Among these applications, bioplastics and biomaterials have a special hemicellulose contribution (Chap. 8). Hemicellulose can be hydrolyzed in oligomers with diverse biological activity (Chap. 9) and also with a recognized potential on food nutrition (Chap. 10). Hydrolyzed hemicellulose into monomeric sugars is a raw material for fermentable processes (Chap. 11) or conversion processes into chemical building blocks (Chap. 12) such as furan compounds (Chap. 13). Hemicellulose-based biomaterials have been already applied in biomedical and pharmaceutical fields (Chap. 14), with a remarkable contribution in chemical/drug delivery systems (Chap. 15).

This book is a joint effort of enthusiastic researchers working on hemicellulose use and the biorefinery process for obtaining high value-added products. This joint effort would not have been possible without the support of many colleagues and collaborators, which is sincerely acknowledged. My gratitude to all the contributors who were excited with the proposal dedicated to compiling their experiences in the chapters, even during the professional/personal challenging period of the COVID-19 pandemic, which paralyzed the world. I am very indebted to my research group from the Laboratory of Biomass Characterization and Conversion (LCCB/IPBEN/Unesp), students from the graduate program of Ph.D. in Bioenergy (Usp, Unicamp, and Unesp), and Applied Microbiology (Unesp). The graduate students (currently develop researches on hemicellulose chemical and biological modifications, bioactive compounds, and use in biomaterials) embraced the idea of writing chapters, strongly contributing to this book. I am very thankful to my family, colleagues, and friends for their constant support and for lending a hand whenever it was needed.

Rio Claro, São Paulo, Brazil Michel Brienzo

# About This Book

Hemicelluloses are plant cell wall polysaccharides, with diverse chemical structures and properties. It is the second most spread and found organic polymer in nature (lignocellulosic materials from agro and industrial wastes) representing a renewable raw material. This book provides knowledge considering studies on hemicellulose production life cycle and aspects of circular economy, and methods of chemical and biological characterization. Biorefinery has an important contribution to hemicellulose production associated with biomass industrial processes. Hemicellulose has been taken as a promissory alternative source of sugars for renewable fuels and a platform for chemicals production. This book reviews chemical processes for sugar production, sugar degradation routes and products, and challenges for pentose fermentation. Various aspects of hemicellulose chemical and biological modifications are presented with a focus on physicochemical properties improvement. Hemicellulose is evaluated as a raw material for bioplastic production, with important concerns on environmental preservation. Besides, hemicellulose is presented as a component of advanced materials for biomedical and pharmaceutical uses, and as a hydrogel for chemicals and drug delivery. This book joins expert's knowledge in biorefinery applications and processes for hemicellulose conversion into high value-added products such as monosaccharides and oligosaccharides, intermediate compounds for a chemical platform, biomaterials, and biofuels.

# Contents

# About the Editor

**Michel Brienzo** is a researcher at São Paulo State University (Unesp), Institute for Research in Bioenergy (IPBEN), working on Biomass Characterization for Bioenergy and Biorefinery and coordinating the Lab of Characterization and Conversion of Biomass. Dr. Brienzo holds a bachelor in Biochemical Engineering with an emphasis in Biotechnology and a Ph.D. grade in Applied Microbiology Sciences from the University of São Paulo (USP). Dr. Brienzo worked as a researcher at the National Institute of Metrology, Quality and Technology (Inmetro), studying the physicochemical characterization of biomass and enzymatic digestibility of lignocellulose (chemistry and enzymology of biomass bioconversion). Dr. Brienzo had a postdoctoral position achieved at Stellenbosch University (South Africa) in the Process Engineering Department studying physicochemical properties of biomass. The focus of his research is mainly on the chemical and physicochemical properties of biomass, polysaccharides extraction, pretreatment, and enzymatic hydrolysis. Special attention is dedicated to hemicellulose in his projects that study its solubilization, conversion into bioactive compounds, and bioplastic/biomaterials production.

# 1 Hemicelluloses Role in Biorefinery Systems of Cellulosic Bioethanol, Particleboard, and Pulp and Paper Industries

Hernan Dario Zamora Zamora, Hamed Olafiku Olayiwola, Ana Paula Jacobus, Jeferson Gross, Luvuyo Tyhoda, and Michel Brienzo

**Abstract**

Hemicelluloses are located in the walls of vegetal cells and are the second most abundant macromolecules in the world. Thanks to the inherent chemical composition, hemicelluloses can be directly used as substrates for enzymes synthesis and in film or polymer manufacture or turned into several products, which include among others biofuels, biopolymers, organic acids, sweeteners, and intermediate bioproducts. However, for the generation of such value-added bioproducts as mentioned above, to succeed, there is a requirement for the development of appropriate conversion paths and processes from hemicelluloses under the realm of the biorefinery concept. One of the major challenges in the conversion of hemicelluloses to bioproducts is due to the inherent links that exist between hemicelluloses and such cell wall components as lignin and cellulose. Due to these links, it is difficult to liberate hemicelluloses from biomass with most processes, most notably the pulping process, without incurring any losses or degradation of structural properties. With the selection and application of appropriate processing routes, most of the hemicelluloses can be recovered, and can serve as precursors or raw materials for the development of value-added products in a biorefinery scheme. The production processes for cellulosic bioethanol, particleboard, and pulp and paper are potential avenues where hemicelluloses can be recovered and upgraded without significant effects on the main process or

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M. Brienzo (ed.), *Hemicellulose Biorefinery: A Sustainable Solution for Value Addition to Bio-Based Products and Bioenergy*, Clean Energy Production Technologies, https://doi.org/10.1007/978-981-16-3682-0_1

product. The most common techniques for hemicelluloses extraction include chemical paths, which are characterized by the use of hydroxides, organic solvents, acids, and peroxides. In the realm of a biorefinery, these techniques can be applied prior to cellulosic bioethanol, pulp and paper or particleboard production to recover hemicelluloses in a much purer form, and high structural integrity in order to be functionalized or converted into bioproducts integrated. In this context, the chapter presents potential avenues for hemicelluloses recovery and application of such recovered hemicelluloses for bioproducts development. The chapter further details specific applications and challenges related to such applications.

**Keywords**

Biomass utilization · Hemicelluloses · Biorefinery · Renewable energy

## 1.1 Introduction

The biorefinery (BRF) concept is of great interest as promising route for bioproducts obtaining from biomass (BS). The central characteristic of the concept is the efficient use of a diverse array of bio-based precursor materials, such as BS, to obtain several classes of value-added bioproducts under an integrated platform or platforms, or simultaneous processes. The BS that is most used under this scheme is the vegetal (VB), which can be gathered from agroindustrial crops or residues from VB processing (Sharma and Saini 2020).

The current dynamics of the global energy consumption points to crude oil as the central and the main source that supports the world energy and chemical supply matrix (in 2019 oil shared 33.1%) (British Petroleum 2020). This is largely due to the fact that oil can be processed through a refinery system that allows production of several chemical products (U.S. Energy Information Administration 2012). However, the drawbacks associated with the use of crude oil including its extraction, refining, and the use of its derivatives are associated with the generation of greenhouse gas emissions, which have huge negative effects to human health and the environment (Hoegh-Guldberg et al. 2018; Guedes et al. 2019). BS, especially from vegetal or animal waste, has become in an alternative raw material to replace oil and other non-renewable resources like coal and natural gas (Felipuci et al. 2020). One of the challenges concerning the use of BS as an alternative to crude oil is the lack of similar processing routes as those of crude oil due mainly to the dissimilarities of the two material respect to structure and properties. The biorefinery concept was therefore born out of this need to develop bioproducts using BS as an alternative feedstock to crude oil, taking advantage of its renewable nature and wide availability (Zamora Zamora et al. 2020).

The biorefinery concept has received tremendous attention in research recently owing to the need to reduce greenhouse emissions from oil-based products. Furthermore, such BS utilized in industries as the pulp and paper, saw milling, board

**Table 1.1** Different mass proportions of cellulose (CL), hemicelluloses (HC), and lignin (LG) in selected waste vegetal biomass (VB)

| Vegetal biomass | CL, % | HC, % | LG, % | References |
|---|---|---|---|---|
| MD2 pineapple leaves | 30 | 37 | 22 | Mansor et al. (2019) |
| MD2 pineapple stem | 37 | 34 | 20 | |
| MD2 pineapple root | 42 | 32 | 19 | |
| Coffee cut-stems | 40.4 | 34 | 10.1 | García et al. (2018) |
| Rice husk | 35 | 33 | 23 | Hafemann et al. (2020) |
| Tamarind husk | 14.9 | 33.4 | 25.8 | Alves et al. (2020) |
| Tamarind seed | 20.9 | 15.8 | 28.8 | |
| Sugar bagasse | 42.8 | 27.6 | 24.2 | Silva et al. (2017) |
| Waste triticale | 31.9 | 25.4 | 18.4 | Kucharska et al. (2020) |
| Meadow grass | 27.1 | 22.6 | 16.8 | |
| Beech | 38.6 | 19.9 | 28.3 | |
| Empty fruit bunches | 30.4 | 19.4 | 33.3 | Coral Medina et al. (2016) |
| Corn straw | 36.2 | 28.1 | 21.9 | Cutrim et al. (2019) |
| Corn cob | 28 | 26.7 | 21.7 | |
| Rice peel | 30.6 | 14.5 | 29.7 | |
| Soy peel | 22.4 | 13 | 17.5 | |
| Cassava peel | 24.2 | 4.9 | 50.7 | |
| Wheat straw | 37.5 | 23.8 | 20.5 | Díez et al. (2020) |
| Pine bark | 21.9 | 18.3 | 40.7 | |
| Spruce bark | 29.7 | 13.9 | 45.1 | |
| Orange bagasse pellet | 5.4 | 13.6 | 6.2 | da Silva et al. (2020) |
| Coffee silver skin | 20.9 | 7.7 | 30.5 | Niglio et al. (2020) |

production, sugar processing has adopted this concept so that they can add value to such BS residue which do not lead to product, as black liquor, saw dust, wood chipping rejects, and bagasse, respectively. BS has a distinct chemical structure, which is principally constituted of water and predominantly of cellulose (CL), hemicelluloses (HC), and lignin (LG) (Ge et al. 2018; Yousuf et al. 2020; Bello et al. 2021). BS composition widely varies due to the vast nature and number of plant species and growing conditions that these plants are subjected to on the planet. Such differences can be seen in Table 1.1, which indicates the proportions of each of the major macromolecules, i.e. CL, HC, and LG of several BS processing residues material on a dry basis.

Although the chemical compositions of LC materials are dissimilar, they share similar functions. The principal constituents (CL, HC, and LG) are located into walls of vegetal cells and have particular tasks that are to protect vegetal cells against fungal and insect attacks as well degradation by UV ray. Furthermore, they facilitate the transport water, nutrients, and minerals (Alberts et al. 2014). From a biological point of view, the LC configuration resulting from its intricate structure allows it to suitably perform its role as discussed above. However, the very same intricate structure is a huge challenge to the processing or separation of the BS components due to the intimate association between CL, HC, and LG, which results in immense resistance to processing (Fülöp and Ecker 2020). The strong association of BS individual components is responsible of its recalcitrance. Therefore, the primary aim of any BS processing endeavor should first be the establishment of suitable processing procedures to overcome its recalcitrance so that individual components can be more accessible and obtained in high yield and quality. These could then be used as feedstocks to different bioproducts (Zoghlami and Paës 2019).

The biorefinery system is mainly comprised of the sugar and the LG platforms. The sugar platform focuses on the development of bio-based products from CL and HC. The LG platform on the other hand focuses on the valorization of LG into various bioproducts. The biorefinery system in both platforms includes two main stages, namely the primary and the secondary biorefinery stages. The primary biorefinery stage emphases on such initial processing steps as pretreatment to change the recalcitrant structure so that it is amenable to further processing via chemicals or enzymes. Alternatively, it is comprised of a fractionation step aimed at separating the individual components so that they can be used as feedstocks downstream. The secondary biorefinery stage is comprised mainly of the conversion of the three main BS macromolecules, i.e. CL, HC, and LG into intermediate and final bioproducts (Zamora Zamora et al. 2020). The mass yields in each stage largely depends on the VB composition and among the three main components, HC has received special attention due to its potential as a raw material for various bioproducts (Delgado-Arcaño et al. 2021; Hill et al. 2021). Figure 1.1 shows the most important direct, primary, and secondary bioproducts that can be obtained from HC utilizing a BRF system.

HC are natural macromolecules constituted by different polymers (mainly xylan, arabinan, mannan, galactan, arabinogalactan, glucomannan, and galactoglucomannan), which in turn, are composed predominantly by monomers of hexoses and pentoses like xylose (XY), arabinose (AR), mannose, galactose, and glucose (Benaimeche et al. 2020). HC composition (dry basis) varies in each plant species and therefore in its respective byproducts. In VB, HC content can range from 5% to 40% (Mansor et al. 2019; Díez et al. 2020). Extracted raw HC (polymers mixture) can be mostly used as gum or emulsification agent and for film production. However, broadening the scope of its application requires the establishment of suitable processing conditions to tailor make its composition of constituent polymers for such applications (Abe et al. 2021; Olorunsola 2018).

## 1.2 Hemicelluloses Valorization in the Cellulosic Bioethanol Production

In a BRF system of LC biomass, the primary biorefinery, which includes, pretreatment as well as the secondary biorefinery step comprising mainly hydrolysis are key stages in the production of intermediate or final bioproducts depending on the processing conditions developed (Sharma and Saini 2020). Generally, physical, chemical, biological or combined methods are performed with the objective of

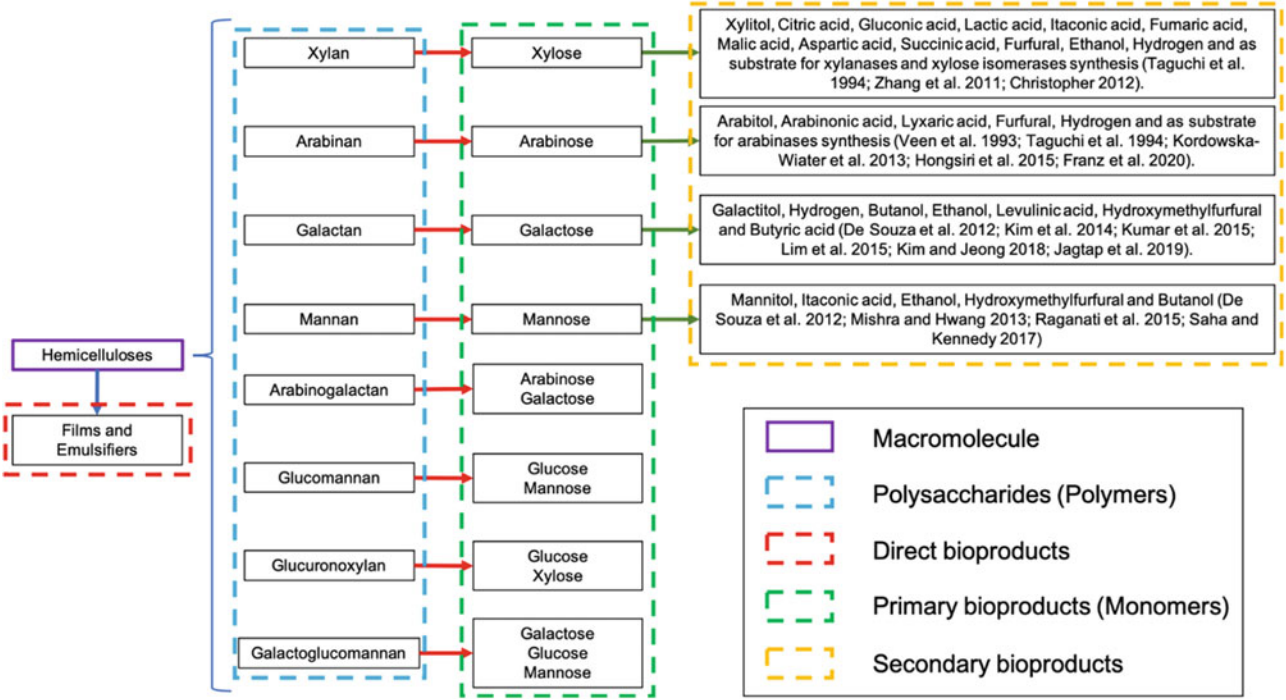

**Fig. 1.1** Main bioproducts developed from hemicelluloses (HC)

enhancing access to the LC structural components through the removal or structural alteration of specific macromolecules contained in the LC biomass (Felipuci et al. 2021; Silva et al. 2017; Shimizu et al. 2020). For example, in second-generation (2G) bioethanol production various pretreatment techniques are applied whose focus is to remove LG and HC are applied. The presence of these components creates a protective barrier to CL, the main precursor macromolecule from which fermentable hexoses are obtained (Naresh Kumar et al. 2019). Although very good results have been obtained with regard to the hydrolysis of CL into hexoses, current works have also focused on the development of new or better techniques for HC conversion as well, thus improving total sugar conversion efficiency and improving global yields in 2G bioethanol production (Guigou et al. 2017).

As discussed previously and also illustrated in Fig. 1.1, HC are considered copolymers constituted by different types of polymers, among them are xylan, arabinan, galactan, mannan, arabinogalactan, glucomannan, glucuronoxylan, and galactoglucomannan (Benaimeche et al. 2020). These polymers are formed through polymerization of monomeric sugar units. These monomers can be the first bioproducts obtained through a BRF system. However, for an efficient conversion of the polymers to monomers to occur, the LC biomass must undergo some sort of physical, chemical or enzymatic treatment (Melati et al. 2019). Based on HC chemical composition, there are two possible ways for improving global yields in 2G bioethanol production. The first one is related to the valorization of HC through direct use in materials or products with emulsifying features. The second pathway is geared towards the conversion of HC through supplementary processes (pretreatment and hydrolysis) to obtain additional bioproducts (Olorunsola 2018; Zhao et al. 2020; Delgado-Arcaño et al. 2021). In both cases (direct uses and supplementary processes), it is necessary to implement a delignification stage, which can be performed prior to or simultaneously with HC extraction (Martino et al. 2017).

The one-pot processing, i.e. direct HC extraction without a separate delignification stage, using an alkaline-peroxide pretreatment, has been shown to efficiently remove LG while extracting HC in one single step. The resulting LC residue has shown good enzymatic digestibility for its subsequent hydrolysis (Melati et al. 2021; Alves et al. 2021). On the other hand, when delignification and HC extraction are performed as separate processes, it is common to complete LG removal first. This can be achieved through alkaline-organosolv delignification at 75 °C, using 30% solvent and 70% alkali concentrations (Farhat et al. 2017). After delignification, HC can be extracted with alkali using low hydroxide concentrations (4–20% at moderate temperatures) and washings with 96% ethanol to precipitate HC (Flórez-Pardo et al. 2018).

Whether one pot or separate treatment process is applied for HC extraction and LG removal, several options of procedures are available for obtaining monosaccharides (xylose, arabinose, mannose, galactose, and glucose). The extraction of XY, for instance, often follows the use of inorganic acid solutions (around 50% of concentration) and low solid loadings in a solid/liquid ratios of 2–8% m/v (Santos et al. 2020). Nevertheless, the acid route is not the only route by which XY can be produced from HC (especially xylan). Enzymatic procedures that break down HC into XY through xylanases treatment of BS have also been successfully applied (Freitas et al. 2021; Forsan et al. 2021; Felipuci et al. 2020). When such enzymatic routes for HC hydrolysis are incorporated in a BRF system, this normally follows two routes; the first one is related to the use of synthesized xylanases from specific LC substrates and specific microorganisms and the second one is based on the use of commercial cocktails of xylanases (Bhardwaj et al. 2019).

Once free XY is obtained through any or combination of the aforementioned processes, it can then be turned into bioethanol through fermentation processes using different strains of *Candida shehatae*, *Pichia (Scheffersomyces) stipitis*, *Spathaspora passalidarum*, *Pachysolen tannophilus* and genetically engineered *Saccharomyces cerevisiae* (Rodrussamee et al. 2018; Robak and Balcerek 2018; Milessi et al. 2020). However, this procedure has shown several issues related to operational conditions, including the microorganism selected and these have an impact of bioethanol yield.

### 1.2.1 Hemicelluloses Recovery in 2G Bioethanol Process

According to diverse studies, 2G bioethanol is not cost-effective yet compared with first generation (1G) bioethanol or electricity production (Losordo et al. 2016). This is because 2G production exhibits low profitability when only 2G biofuel is produced. This relates manly to such factors as the high enzymes cost, costs attributed to energy consumption in different stages (mainly pretreatment and hydrolysis) as well loss of potential revenue as a result of non-utilization of byproducts with high potential to be turned into products (Zhang 2019). In order to deal with these financial drawbacks, economic models can be used to predict business favorable scenarios when 2G processes are incorporated to 1G processes or when other processes aimed at adding value to side streams are incorporated (Junqueira et al. 2017; Coral Medina and Magalhaes 2020).

In the 2G bioethanol framework, one of the main objectives is to deconstruct LC biomass and to try to remove LG and HC through different techniques. However, from the BRF point of view both LG and HC can have value as raw materials for obtaining several value-added bioproducts using suitable procedures (Sharma and Saini 2020). In the HC case, it is possible to obtain xylitol, citric acid, gluconic acid, lactic acid, itaconic acid, fumaric acid, malic acid, aspartic acid, succinic acid, furfural, bioethanol, and hydrogen from XY (Taguchi et al. 1994; Zhang et al. 2011; Christopher 2012). Arabitol, arabinonic acid, lyxaric acid, furfural, hydrogen from AR (Veen et al. 1993; Taguchi et al. 1994; Kordowska-Wiater et al. 2013; Hongsiri et al. 2015; Franz et al. 2020). Galactitol, hydrogen, butanol, bioethanol, levulinic acid, hydroxymethylfurfural, and butyric acid can be obtained from galactose (De Souza et al. 2012; Kim et al. 2014; Kumar et al. 2015; Lim et al. 2015; Kim and Jeong 2018; Jagtap et al. 2019). Mannitol, itaconic acid, bioethanol, hydroxymethylfurfural, and butanol can be obtained from mannose (De Souza et al. 2012; Mishra and Hwang 2013; Raganati et al. 2015; Saha and Kennedy 2017).

Continuing with BRF context, some works have analyzed several methods for simultaneous breaking down of HC and CL into pentoses and hexoses using different kind of pretreatments (physical, chemical, biological or combined). Classical acid pretreatments using diluted conditions (0.1–10%) at mild temperatures (100–250 °C) allow for production of sugar monomers while reduce fermentation inhibitors from forming (Baruah et al. 2018). Modified Fenton pretreatment (peroxide + chloride + solvent), at 130 °C, 1.5 bar and short reaction times (0.5–4 h) exhibits high yields of carbohydrates recovery (94%) in saccharide solution (that subsequently is driven to hydrolysis and fermentation) and allows a separation of up to 87% of LG by simply filtration. Steam explosion pretreatment catalyzed by acid catalysts is of particular importance as it contributes to maximize HC solubilization in water and its subsequent conversion into hexoses and pentoses through hydrolysis of glycosidic bonds in CL and HC (mainly in HC), which improves efficiency of polysaccharides recovery/separation (Robak and Balcerek 2018). Its common configurations are of high pressure (0.5–5 MPa), moderate temperature (150–270 °C), and low retention times (1–10 min) to prevent inhibitors formation (Yu et al. 2018).

Finally, it is important to mention that depending on chemical pretreatments performed for taking advantage HC, HC-based products can have different characteristics. For instance, if diluted acid methods are applied, then the main obtained bioproducts will be XY and xylooligosaccharides. If on the other hand alkali procedures are performed, then the polymeric form of XY will be extracted (Brienzo et al. 2016).

## 1.3 Hemicelluloses Valorization in the Pulp and Paper Industry

The increasing demand of products from virgin feedstocks and the resultant pressure on the environment has expanded the concept of biorefinery which is based on exhaustive utilization of feedstocks. The implementation of biorefinery concepts in the pulp mills leads to sustainable co-production of paper, fuels, power and valuable chemicals from different LC materials (Vena 2013). In the standard kraft pulping process a significant quantity of HC which is equivalent to about 15% of the feedstock is dissolved into the black liquor (Christopher 2013). The black liquor is recycled back to the reboiler for combustion due to the high heating value of dissolved LG (about 26.9 MJ/kg), but the low heating value of HC (about 13.6 MJ/kg) makes it underutilized when incinerated in the boiler. Hence, pre-extraction of HC prior to pulping entails important economic benefits by offering more valuable alternative in generating additional streams of high value products (Um and van Walsum 2010). They have excellent potentials in food and pharmaceutical industries (Joubert et al. 2016).

The extraction of HC from the feedstock has both advantages and disadvantages on the final pulp and paper, depending on the extraction methods and the pulping process. Common extraction methods include steam, hot water, dilute acid, and alkaline treatments (Al-Dajani et al. 2009; Kämppi et al. 2010; Lei et al. 2010). Hot

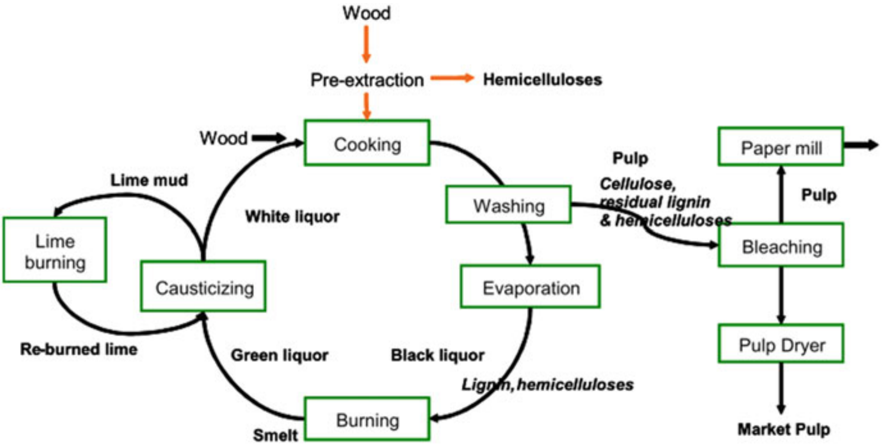

**Fig. 1.2** Extraction of HC prior to kraft pulping process (Vena 2013)

water and acid methods produce higher HC yields, but the severity of the treatments may reduce the final pulp yield and paper quality (Mendes et al. 2010; Vena 2013). HC recovery vary considerably during alkaline extraction, but the effect on the pulp yield reduction is minimal (Al-Dajani et al. 2009; Jun et al. 2012; Vena 2013). Pre-extraction prior to pulping increases delignification which causes reduction in chemical consumption during cooking and bleaching stages (Kautto et al. 2010; Yoon et al. 2011). Despite this benefit, its removal could have detrimental effects as it contributes to pulp quality. HC has a high affinity for water molecules which improves pulp beatability (Ban et al. 2011). It also improves the tensile, burst and tear strength of paper products by serving as an inter-fiber binding agent (Lima et al. 2003; Schönberg et al. 2001).

As discussed in the above section, HC extraction can be integrated into the pulping process (Vena 2013; Joubert 2016) (Fig. 1.2). According to Postma et al. (2014), the extracted HC can be functionalized into a product which can be used as an additive in paper making. The authors extracted 4-*O*-methyl glucuronoxylan (Me-GluX) from Eucalyptus grandis, under mild alkaline conditions, which was cationized and added to *E. grandis* bleached kraft pulp before refining. This resulted in improved tensile, burst and tear strength when compared to cationic starch. Therefore, in order to fully harness the potentials HC pre-extraction and pulping, a combined approach requiring optimization of pre-extraction conditions and pulping process with minimal degradation of the CL component should be prioritized (Vena 2013).

## 1.4 Hemicelluloses Valorization in Particleboard Fabrication

Wood fibers are incorporated into polymeric resins, thermoplastics, and inorganic binders in a bid to produce low cost, sustainable building components, or as a means of adding values to secondary materials. Their unique attributes such as low cost, biodegradability, sustainability, low density, and good mechanical properties make them suitable alternatives to synthetic reinforcements in composite panel construction. The cell wall of wood is composed of CL, HC, LG, extractives, and minerals in varying compositions. The influence of the components is dependent on the type of the binder. In polymeric and thermoplastic matrices, the susceptibility of wood to water uptake and fungal decay is the major challenge. HC are the most hydrophilic wood components and are responsible for high water affinity in thermoplastic binder (Pelaez-Samaniego et al. 2014; Pereira Ferraz et al. 2016). Moisture uptake causes swelling which stresses the interfacial fiber-plastic bonds (Pelaez-samaniego et al. 2013). In inorganic matrices, the HC and extractives inhibit setting and are well-known causes of wood-cement incompatibility. They promote the formation of impermeable shields around non-hydrated cement grains, depriving them access to water, thereby impairing fiber-matrix bond (Quiroga et al. 2016).

Pretreatment of wood to remove or modify the hydrophilic and inhibitory components becomes mandatory to improve their performance in the different matrices. The treatments include thermal and chemical or a combination of both processes. Thermal treatment involving aqueous hot water extraction removes sugars, and other inhibitory water soluble compounds (Pelaez-samaniego et al. 2013; Quiroga et al. 2016). It reduces the hygroscopicity, improved the crystallinity of CL, enhance the dimensional stability and resistance to degradation (Pelaez-samaniego et al. 2013). Hot water extraction is the most environmentally treatment as it does not require additional chemicals (Garrote et al. 1999). Chemical treatments include alkalization, acetylation, methylation, cyanoethylation, and sulfuric acid treatment (Bledzki et al. 2008; Oladele et al. 2015). Alkalization delignifies the sample and degrades the HC into non-inhibitory substances (Quiroga et al. 2016). Other chemical treatments such as acetylation and methylation modify the BS components to become more hydrophobic, thereby improving their durability and dimensional stability. Acetylation causes the hydroxyl groups in amorphous CL, LG, and HC with acetyl group, thereby reducing the available sorption sites on the fiber surface (Bledzki et al. 2008).

Pelaez-Samaniego et al. (2014) incorporated hot water extracted hardwood and softwood chips in polymeric resin (Urea Formaldehyde) matrix and concluded that the removal of HC improved the dimensional stability of the boards. Although the effect was not significant on the mechanical properties, the removal of HC promoted easier compression and flexibility of the fiber. A similar observation was reported in a separate study where hot water treated pine particles were encapsulated in PP and HDPE matrices (Pelaez-samaniego et al. 2013). The treatment had significant effect on the moisture resistance of the boards and had an overall positive impact on the board quality. Extraction of HC from anaerobic digested dairy fibers incorporated into HDPE reduced the hydrophilicity of the fibers and improved the stiffness and

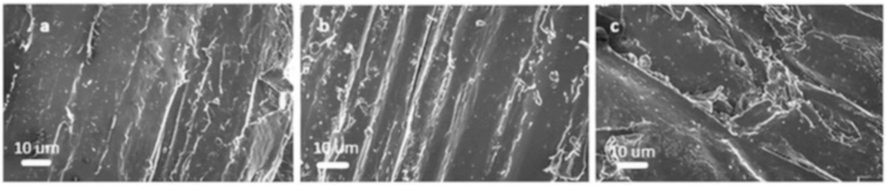

**Fig. 1.3** SEM micrograph of (**a**) untreated, (**b**) hot water extracted and (**c**) alkalized bagasse fibers (Amiandamhen et al. 2018)

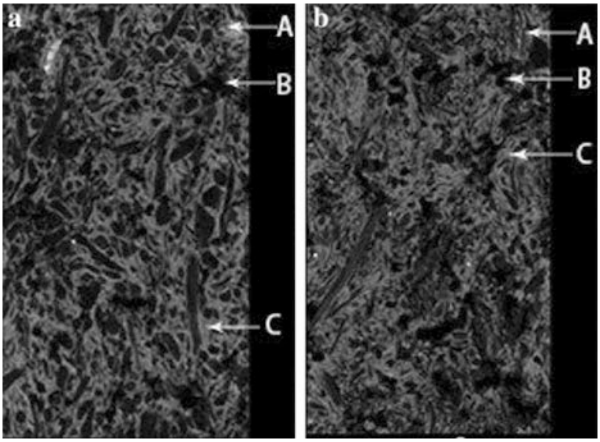

**Fig. 1.4** 2D segmentation of bagasse panel untreated (**a**), alkali treated (**b**) (A fibers, B voids, C matrix) (Amiandamhen et al. 2018)

mechanical strength of the boards by 30% and 36%, respectively (Pereira Ferraz et al. 2016).

Enhancement of properties of inorganic-bonded particleboards have also been reported. Amiandamhen et al. (2018) incorporated pretreated natural fibers into phosphate-based inorganic binder. The treatment influenced the fiber properties and improvement was observed in all the properties evaluated. It was recommended that a mild alkaline treatment is sufficient to improve the properties of the boards.

As shown in the SEM images in Fig. 1.3, the authors posited that apart from altering the chemical compositions of the fiber, treatment methods removed other impurities such as waxes and pectin. The 2D segmentation image shown in Fig. 1.4 indicated that the removal of the impurities, as a result of the pretreatment, enhanced the bonding between the fibers and the binder. The modulus of rupture of untreated bagasse boards increased from 150 to 175 MPa after alkali treatment. This also caused a reduction in the water absorption potential of the boards by 33%. It was recommended that a mild alkaline treatment is sufficient to improve the properties of the boards.

A similar observation has been reported in geopolymer bonded wood composites (Olayiwola 2021; Asante 2020). Olayiwola et al. (2021) reported that unlike in ordinary Portland cement, the presence of HC did not prevent geopolymer setting,

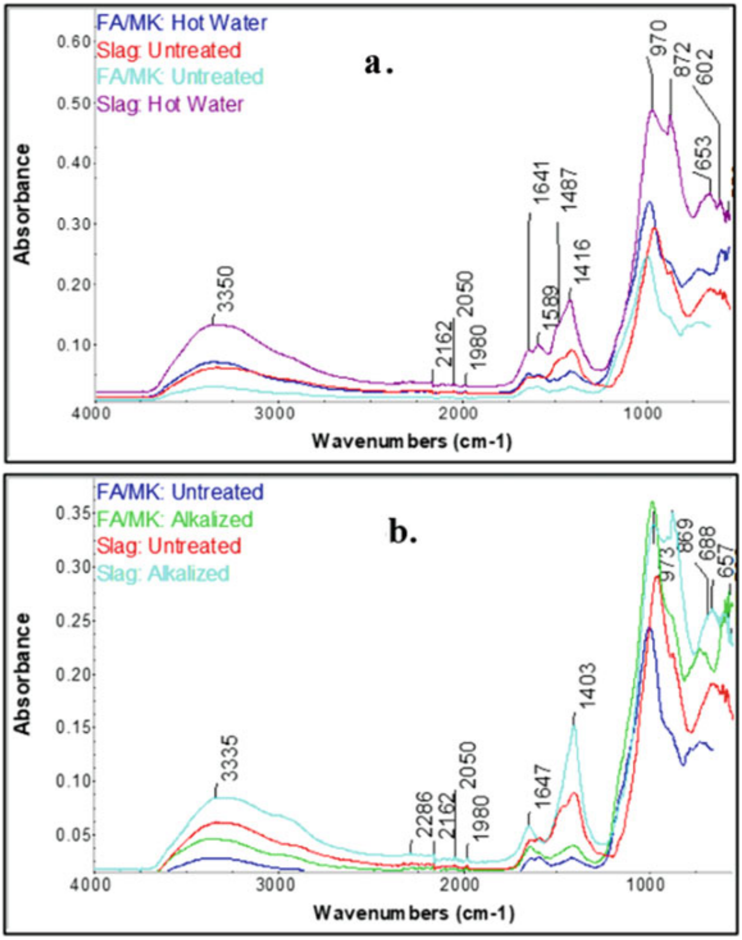

**Fig. 1.5** FTIR spectra of untreated bagasse fibers, hot water extracted (**a**) and mild alkali treated (**b**) in fly ash-metakaolin and slag based geopolymer matrix (Olayiwola 2021)

but lowered the reaction kinetics. The reaction improved after pretreatment. The FTIR spectra shown in Fig. 1.5 indicated formation of new geopolymeric products, which confirms the observation that pretreatment enhanced the geopolymerization reactions. Mild alkali treatment of *A. mearnsii* particles incorporated in a 100% slag based geopolymer increased the modulus of rupture of the panels by 23.94% (Olayiwola 2021).

While the discussion above focuses solely on the removal of HC to improve fiber properties, a few studies are now reporting on value addition on such extracted HC. Soludongwe (2020) examined the co-production of furfural from extracted XY and wood composites from the remaining wood residue in a manner resembling a process called value prior pulping (VPP) in the pulp industry. Through this

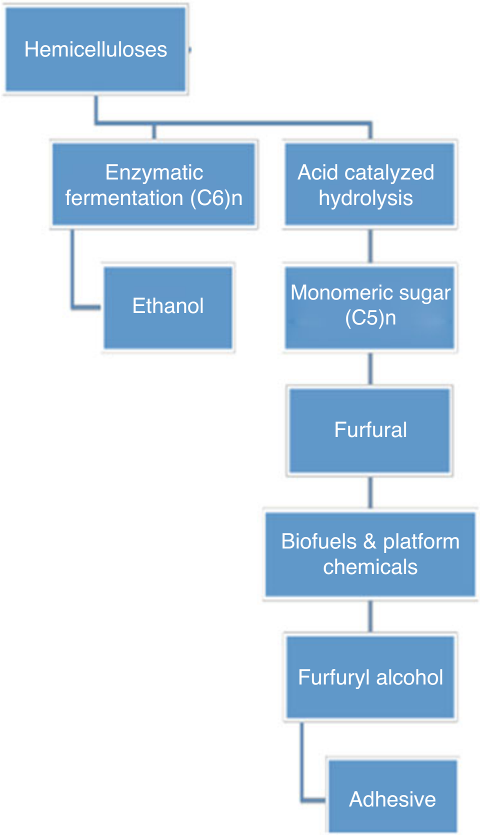

**Fig. 1.6** Different bioconversion pathways of HC. (Adapted from Soludongwe 2020)

approach, HC was extracted and then used a raw material to produce furfural. The furfural would then be functionalized to produce a furfural-based binder, which then could be used to bind BS particles during composite product production. This shows that pretreatment, in addition to improving BS properties, could also be used to produce raw materials such as furfural which finds wide application in foundry and furfural-based binding derivatives (Binder et al. 2010; Orlova 2016). Orlova (2016) developed a furfural-based binder which had good polymerization, polycondensation, and hardening properties. The binders could find applications in producing caulking compound, putties, and chemically resistant gaskets and joints. Figure 1.6 shows the different pathways of bioconversion of HC.

## 1.5 Challenges of Biological Aspects of Pentoses Fermentation of Lignocellulosic Hydrolysates Using *Saccharomyces cerevisiae*

The biofuel industry in Brazil stands as one of the most successful in the world with regard to cost-effective bioethanol generation from sugarcane. The bioethanol (first generation) is based on fermentation of sugars (mainly sucrose) derived from the soluble fraction of processed sugarcane plants using *Saccharomyces cerevisiae* (Basso et al. 2013; dos Santos et al. 2016a). Despite the easy access to available hexoses, there is a fraction of sugars that still are unavailable for conversion in the sugarcane BS, which if converted would lead to an increase in bioethanol yield. These sugars are not soluble, but being part of a complex structure, as glycoside molecules, on the plant cell wall (known as lignocellulose) (Basso et al. 2013; Isikgor and Becer 2015; dos Santos et al. 2016a). Typical plant BS contains approximately 40–50% CL, 20–40% HC, and 20–35% LG (Liao et al. 2016). According Nunes et al. (2020), sugarcane bagasse is, on average, made up of 42.2% ± 1.93 CL, 27.6% ± 0.88 HC, 21.6% ± 1.67 LG, 5.63% ± 2.31 extractive compounds (sugars), and 2.84% ± 1.22 ash. Considering that 140 kg of dried bagasse is produced per ton of processed sugarcane in the 2020/2021 sugarcane season, in Brazil, were harvested 665.105 million of tons of sugarcane producing 93.114 million of tons of dry bagasse (Pereira et al. 2015; CONAB 2020). In addition, only 32 million of liters from cellulosic bioethanol (2G) were estimated to be produced in 2020 contrasting with 31.35 billion liters from 1G bioethanol in Brazil (USDA 2020).

There is still a huge opportunity to grow on cellulosic bioethanol production. However, challenges relating to economic and technical factors still need to be resolved. Among the technical challenges is the realization of efficient plant BS deconstruction techniques with cost-effective enzymatic treatments as well as an efficient implementation of large-scale fermentations in industrial settings (Basso et al. 2013; dos Santos et al. 2016a). Another important limitation is that *S. cerevisiae* does not have the metabolic arsenal to convert pentoses, which comprise an economically relevant fraction of sugars released from cellulosic BS (Basso et al. 2013; dos Santos et al. 2016a). In the LC biomass the amounts of D-XY and L-AR, derived from HC and pectin polymers in plant BS, account for 10–25% and 2–3%, respectively, of the carbohydrate content of LC feedstocks (Lynd 1996). That problem has been addressed by genetically engineering yeasts for efficient conversion of XY and AR into bioethanol (Demeke et al. 2013; dos Santos et al. 2016b) that will be shortly described below. Nevertheless, one of the remaining complications for implementation of a 2G bioethanol production is the significant inhibition of yeast fermentation by toxic compounds derived from lignocellulose polymers (Basso et al. 2013; Isikgor and Becer 2015; dos Santos et al. 2016a).

### 1.5.1 Yeast Engineering For Second Generation Bioethanol

For many decades, researchers have been exploring ways to increase the efficiency of pentose-fermentation/ethanol production using *Saccharomyces cerevisiae*. Recently, this quest has benefitted from the availability of such advanced tools as genomics (whole-genome sequencing, QTL analysis), genome editing, evolutionary engineering (metabolic engineering, experimental evolution), and protein engineering (Jansen et al. 2017). The strategy to build yeast strains that are capable to consume XY and AR addresses is based in to link the sugars up taking with glycolysis producing bioethanol economically worthwhile.

#### 1.5.1.1 Xylose Fermentation

For D-XY, researchers described that two modifications are necessary (Jeffries and Jin 2004; Van Maris et al. 2007). The first involves the conversion of XY into D-xylulose through a heterologous pathway. The second focuses on the modification of *Saccharomyces cerevisiae* xylulokinase and non-oxidative pentose phosphate pathway (PPP). For conversion of XY to D-xylulose two strategies were developed; i.e., one that relies on simultaneous expression of a heterologous xylose reductase (XR) and xylitol dehydrogenase (XDH). This is the strategy found in some yeast and filamentous fungi. The other approach is related to the expression of a heterologous xylose isomerase (XI), mechanism from procaryotes, mainly (Hahn-Hägerdal et al. 2001) (Fig. 1.7).

The first attempt was to engineer XR and XDH focused on using those enzymes from xylose-metabolizing yeast *Scheffersomyces stipitis* (Kötter and Ciriacy 1993). Having *S. stipitis* as the donor organism and based on its capability to utilize NADH in the XY reduction step. However, the recombinant *S. cerevisiae* expressing heterologous XR/XDH have resulted in low bioethanol yield and xylitol by-product formation (undesirable). This was found to be partially related to unfavorable thermodynamic properties of the reactions and that the worth nothing that first reaction (XR) preferably consumes NADPH, whereas the second reaction (XDH) exclusively produces NADH, which is not regenerate in anaerobic conditions. When less NADH is consumed in the XR reaction, then less NAD+ is available for the XDH reaction. If the amount of NAD+ is insufficient, xylitol is increased (Bruinenberg et al. 1983; Rizzi et al. 1989).

Many strategies were developed to counterpart this setback. Among them was introducing a change in activity ratios for XR and XDH compensating the equilibrium constants. With this goal yeast strains with higher XDH activity than XR which works, when the high activity of XDH less xylitol was formed were built (Walfridsson et al. 1997). To this equation another enzyme was added. A third step (xylulose kinase) XK, the enzyme which phosphorylates xylulose to xylulose 5-phosphate, and was determined that the optimal XR:XDH:XK ratio was 1:10:4 for minimal xylitol formation and confirmed that a decreasing XR:XDH ratio correspondingly decreased xylitol and acetate formation and increased bioethanol production. Overproduction of XK also enhanced the specific XY consumption (Hahn-Hägerdal et al. 2001).

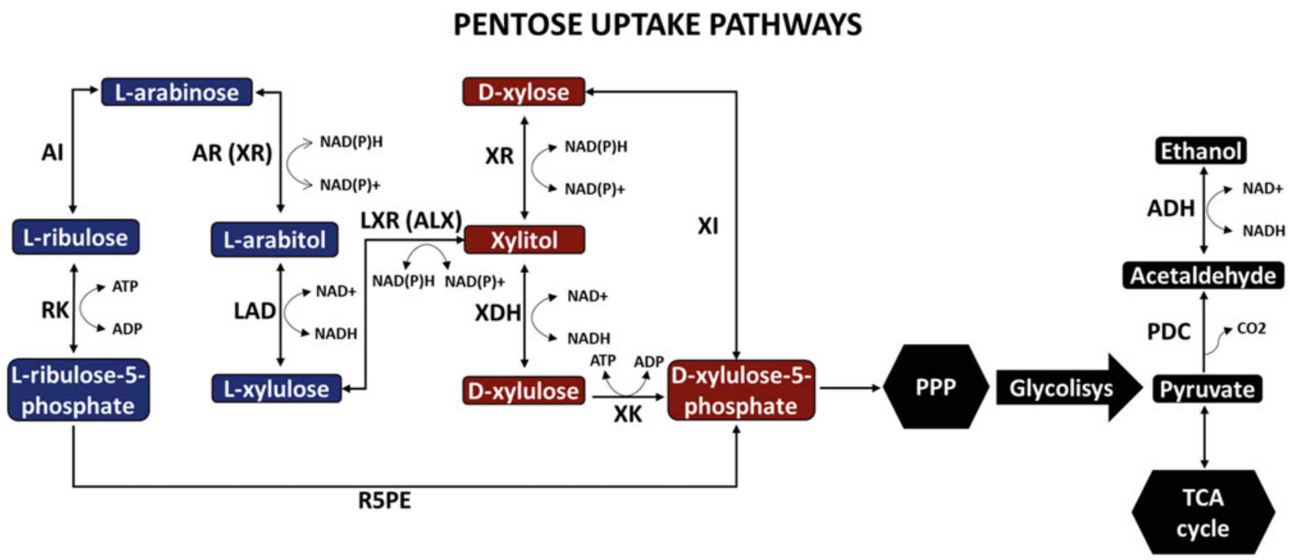

**Fig. 1.7** Representative scheme of pentose uptake/fermentation pathways. The figure shows metabolic oxireductase and isomerase pathways for Arabinose (blue) and Xylose (red) in fungi and bacteria, and central metabolism (black). *AR(XR)* Aldose reductase, *LAD* L-arabitol-4-dehydrogenase, *LXR(ALX)* L-xylulose reductase, *XDH* D-xylulose reductase, *XK* Xylulokinase, *AI* L-arabinose isomerase, *RK* L-Ribulokinase, *R5PE* L-Ribulose-5-P-4-epimerase, *PDC* pyruvate decarboxylase, *ADH* alcohol dehydrogenase, *PPP* phospho pentose pathway, *TCA cycle* tricarboxylic acid cycle

Other approaches, such as Fusion Protein or Site-Specific Mutagenesis, but without greater success were used. On top of that, *S. cerevisiae* have a gene *GRE3*, that encodes a NADPH-dependent aldose reductase that can convert XY to xylitol (Kuhn et al. 1995). The activity of this enzyme could impair the redox balance, accumulating more xylitol resulting in a decrease in XY fermentation. To overcome that, the removal of *GRE3,* and genetic modifications aimed at increasing cofactor regeneration resulted in a decrease in xylitol accumulation while increasing bioethanol production (Träff et al. 2001; Verho et al. 2003; Romaní et al. 2015; Costa et al. 2017; Cunha et al. 2019).

The second strategy to link XY with glycolysis is to use XI enzyme. This approach has the advantage of being a one-step reaction that directly converts XY to xylulose without cofactor requirement (Zhou et al. 2012; Kwak and Jin 2017). The XI catalyzes the reaction in a reversible way involving the isomerization of XY and D-glucose to D-xylulose and D-fructose, respectively. Previous study of to express xylose isomerase from bacteria from *Actinoplanes missouriensis* (Amore et al. 1989) and *Clostridium thermosulfurogenes* (Moes et al. 1996) did not show expression of the protein despite the mRNA's being detected. Other attempts based on the use of XI from *E. coli* (Sarthy et al. 1987; Ho 1989) and the *Bacillus subtilis* (Amore et al. 1989), heterologous expression of the gene directed synthesis of mostly insoluble protein, catalytically inactive. *Termus thermophilus* XI was expressed successfully in *S. cerevisiae* but at low levels and xylitol by-product accumulation was observed (Walfridsson et al. 1996). The problem was solved with expression of a xylose isomerase from the fungus *Piromyces* sp. leading to an efficient XY fermentation (Kuyper et al. 2003).

The xylose isomerase from *Lachnoclostridium phytofermentans* expressed with highly efficient in *S. cerevisiae* (Brat et al. 2009), among others such as from *Orpinomyces* sp. *ukk1*, *Ruminococcus flavefaciens*, *Prevotella ruminicola TC2–24*, *Burkholderia cenocepacia J2315*, *Ruminiclostridium cellulolyticum H10,* and *Streptomyces rubiginosus*, as reviewed and tested by Seike et al. (2019). The development of XI strains was completed with extensive mutagenesis and evolutionary engineering (Demeke et al. 2013). Shortly, combination between expression of XI from fungi and overexpression of *S. cerevisiae* genes encoding xylulokinase and non-oxidative PPP enzymes enabled anaerobic yeast growth on XY (Harhangi et al. 2003). The deletion of *GRE3* gene and encoding an aldose reductase resulted in the reduction of xylitol formation and thereby increasing bioethanol yields on XY fermentation (Kuyper et al. 2005). Using multicopy XI expression cassettes, with optimum codon usage and mutagenesis improved the efficiency of XY fermentation (Lee et al. 2012). Mutations on PHO13 phosphatase resulted in increased fermentation efficiency on XI and XR/XDH which are related to upregulation of PPP genes (Xu et al. 2016). Likewise, there are the identification of other relevant mutations in evolved strains, in genes associated in iron–sulfur cluster assembly, in the mitogen-activated protein kinase signaling pathway and identified mutations affecting intracellular homeostasis of Mn2+ (dos Santos et al. 2016b; Sato et al. 2016; Verhoeven et al. 2017).

#### 1.5.1.2 Arabinose Fermentation

L-Arabinose is a five-carbon sugar found more abundantly in nature as an L isomer, which differentiates it from the other sugars which are most commonly in D form (Ye et al. 2019). While L-arabinose from LC biomass derived from HC and pectin correspond at 2–3% of the carbohydrate content of LC feedstocks (Lynd 1996) and approximately 0.2%, g/g dry weight, L-arabinose content in various fruits and vegetables ranges from 3.3 to 21. 6 g/L (Ye et al. 2019). Fruit processing wastes are high in pectin (12–35%, g/g dry weight) with much less LG content (approximately 2%, g/g dry weight) than LC biomass (Edwards and Doran-Peterson 2012), showing an important niche of wastes as biofuel or biomaterial sources research. Likewise, is stated that in corn fiber hydrolysates and in sugar beet pulp, the amount of L-arabinose is 26% of the total sugar content (Lynd 1996; Grohmann and Bothast 1997).

Arabinose metabolic pathways of native fungal and bacterial strains can be divided into the oxidoreductase and isomerase pathways, respectively (Fig. 1.6). In these two pathways, L-arabinose is converted into D-xylulose-5-phosphate and then metabolized by the non-oxidative PPP (Hahn-Hägerdal et al. 2007) or by the phosphoketolase pathway (Servinsky et al. 2012).

Fungal L-arabinose and D-xylose pathways share three enzymes: arabinase (L-arabinose specific XR), XDH, and XK. However, the conversion of arabinose into D-Xylulose, different from D-xylose, needs two reduction and two oxidation reactions, i.e., (a) NAD(P)H-specific aldose reductase (AR or XR), (b) NAD+-specific L-arabitol-4-dehydrogenase (LAD), (c) NAD(P)H-specific L-xylose reductase (LXR or ALX), and (d) NAD+-specific xylitol dehydrogenase (XDH) (Hahn-Hägerdal et al. 2007). The AR reductase enzyme usually prefers NADPH, while the dehydrogenases strictly use NAD+ (with variation among other fungal species). However, in anaerobioses the production of NAD+ is limited, depending on oxygen (mitochondrial electron chain) and thus impairing bioethanol production (Dien et al. 1996; Kurtzman and Dien 1998).

Because of this difficulty related to redox balance in fungal oxidoreductase pathway, the strategy to produce a L-arabinose fermenting strain relies on the bacterial pathway that converts L-arabinose into xylulose-5-phosphate, including L-arabinose isomerase (AraA), L-ribulokinase (AraB), and L-ribulose-5-phosphate-4-epimerase (AraD) (Lee et al. 1986). This pathway, followed by the non-oxidative PPP and glycolysis allows the L-arabinose fermentation and subsequently ethanol production with equilibrium or neutral redox balance. These enzymes are heterologously expressed in *S. cerevisiae* and could be from different origins such as araA gene from *Bacillus subtilis* (Becker and Boles 2003), *Bacillus licheniformis* (Wiedemann and Boles 2008; Wang et al. 2019), and *Lactobacillus plantarum* (Wisselink et al. 2007; Wang et al. 2013). The araB and araD genes can be from *Escherichia coli* (Wiedemann and Boles 2008; Wang et al. 2019) or *L. plantarum* (Wisselink et al. 2007; Wang et al. 2013). Other approaches to improve L-arabinose fermentation have been tested. These include the overexpression of the non-oxidative PPP genes (*TAL1, TKL1, RPE1,* and *RKI1*), co-expression of L-arabinose fermenting enzymes in *S. cerevisiae* with araA from *E coli* with the groEL and groES chaperonins and adaptive evolution strategies (Becker and Boles 2003; Wisselink et al. 2007; Wiedemann and Boles 2008).

#### 1.5.1.3 Engineering Pentose Transports in *S. cerevisiae* Strains

In yeasts, the main monosaccharides transporters are the major facilitator superfamily (MFS). These facilitation diffusion permeases are classified as uniport, symport (coupled to an ion transport), and antiport, and consist in two sets of six hydrophobic transmembrane-spanning α-helices connected by a hydrophilic loop (Nijland and Driessen 2020). There are no specific pentose transporters in *S. cerevisiae*. The pentoses can be internalized using the native hexoses transporters but with much less efficiency than hexoses. In *S. cerevisiae* are 18 Hxt (hexoses) transporters (Hxt1–17 and Gal2) in which the Hxt1p, Hxt2p, Hxt4p, Hxt5p, Hxt7p, and Gal2p can also transport D-xylose (Bueno et al. 2020). Meanwhile the *Km* values for these pentoses are one to two orders of magnitude higher than for glucose (Farwick et al. 2014). The galactose transporter Gal2 also has a higher *Km* for L-arabinose than for glucose (Subtil and Boles 2012).

All this together means that cells might only start transporting D-xylose and L-arabinose once D-glucose is decreased outside the cells. This feature not suitable for an industrial bioethanol process based on co-consumption of the sugars available to ferment. With the high *Km* values for Hxt transporters for pentoses, the sugar fermentation is slowed down during the pentose-fermentation phase called "Tailing effect." This sums up with the accumulation of ethanol and the reduction of inhibitor tolerance in *S. cerevisiae* at low sugar fermentation rates. This describes the difficulties for the whole scenario for pentose transport in *S. cerevisiae* naturally (Jansen et al. 2017).

In order to improve the co-consumption and transport of pentoses during the fermentation, several studies aimed at developing a specific pentose transporter from a heterologous source *S. cerevisiae* with have been embarked on (Nijland and Driessen 2020). As reviewed by Jansen et al. (2017) and Nijland and Driessen (2020), low-, moderate-, and high-affinity pentose transporters from pentose-metabolizing filamentous fungi or non-*Saccharomyces* yeasts have been functionally expressed in *S. cerevisiae,* and their expression and activity were improved by direct evolution or evolutionary engineering.

In heterologous expression of xylose transporters in *S. cerevisiae*, some processes do result in an increase in xylose uptake. These include the Gxf1 from *Candida intermedia* which has a twofold lower *Km* value for D-xylose transport, which increases xylose consumption, but only in low concentrations of the sugar (4 g/L) (Runquist et al. 2009). From *Arabidopsis thaliana*, a xylose transporter homolog based on a sequence similar to xylose–H+ symporter At5g59250 shows a slight improvement in the D-xylose uptake kinetics (Runquist et al. 2010). In addition, several transporters were studied (Sut1, Sut2, Sut3, Xut1, Xut3, Hxt2.6, Qup2) from *Scheffersomyces stipitis*, a well-known xylose fermenting organism. The Sut1, Sut2, and Sut3 encoding glucose transporters that showed lower *Km* (at mM range) for xylose compared to glucose in *hxt* null *S. cerevisiae* strains and Sut1 also demonstrated increasing the D-xylose uptake ability and ethanol yield during

D-xylose fermentation similar to glucose (Katahira et al. 2008). Xut1 and Xut3 transporters did uptake xylose alone and in co-fermentation with glucose and in a *S. cerevisiae* strain transformed with a genomic DNA library from *S. stipitis* were identified Xut1, Hxt2.6, and Qup2 as promising xylose transporters in an experiment in which the strains were screened in sustaining growth on D-xylose (de Sales et al. 2015).

An arabinose:H+ symporter (BsAraE) from the *Bacillus subtilis* was expressed in a null *hxt S. cerevisiae* resulting into a fourfold D-xylose consumption increase. However, xylitol production was also observed. These strains also consumed xylose with all Hxt transporters in place (Kim et al. 2015). Bueno et al. (2020) have searched in diverse microbiomes, such as the digestive tract of plague insects, and isolated several yeast species capable of using xylose. In *Candida sojae* they found potential high-affinity transporters, of which the Cs4130 was able to consume xylose in high concentration (50 g/L). However, glucose fermentation inhibition also occurred by competition, a known fact for these transporters. In co-fermentation xylose/glucose had demonstrated the same profile as the previously described, using glucose (first 10 h) first) then xylose fermentation.

In the case of L-arabinose uptake, less is known probably because it has less economic impact so far. As it is described above, Gal2 (galactose permease) is the arabinose preferential transporter in *S. cerevisiae*. If the Gal2 is deleted, the cell was found to abolish the L-arabinose transport (Wisselink et al. 2007), and with the overexpression of Gal2 this transport was increased (Becker and Boles 2003). The L-arabinose uptake is also inhibited by competition with glucose that is preferentially transported by Gal2. Some strategies were applied to improve the flux of L-arabinose through known transporters, for example, mutation on Gal2 substrate binding site (F85G). This F85G mutation was associated with an increase in the L-arabinose transport activity and on the counterpoint reduction on specificity of the transporter for D-glucose and D-xylose occurred (Wang et al. 2017a). A mutation found in a genome sequencing of evolved D-glucose-phosphorylation-negative *S. cerevisiae* cells growing in xylose/glucose/arabinose, N376 of the Gal2, was found to decrease the affinity and *Vmax* for glucose, while it also resulted in an increase in L-arabinose transport (Wisselink et al. 2014). Subtil and Boles (2011) demonstrated two arabinose transporters with high transport affinity derived from *Scheffersomyces stipitis* (AraT) and from *Arabidopsis thaliana* (Stp2). Both transporters could mediate the entrance for only L-arabinose but not other sugars such as glucose. They found that *S. cerevisiae* with all Hxt transporters deleted and with bacterial L-arabinose pathway expressed could no longer grow with arabinose being the only carbon source. This was possible only when other glucose transporters (Gal2, Hxt9 e Hxt10) were expressed and with supplemented media such as maltose. They suggested that together with Gal2, this set of transporters can be used for industrial purposes.

Other heterologous arabinose transporters have been identified from *Neurospora crassa* and *Myceliophthora thermophile* (Li et al. 2015), and *Penicillium chrysogenum* (Bracher et al. 2018). However, but it was established that glucose/xylose competition on those transporters favored the hexoses and still no heterologous pentose transporter was reported to either improve L-arabinose fermentation or allow arabinose and glucose simultaneous fermentation (Ye et al. 2019).

## 1.6 Yield Loss Through the Formation of Inhibitors During the Hydrolysis of Lignocellulose Materials

The key polymers comprising the lignocellulose fraction of plants are represented by the CL (D-glucose units condensed through β(1→4)-glycosidic bonds), the HC (xylan, galactomannan, glucuronoxylan, arabinoxylan, glucomannan, and xyloglucan), and the LG (originated from the phenylpropanoid units *p*-coumaryl alcohol, coniferyl alcohol, and sinapyl alcohol) (Kumar et al. 2009; Isikgor and Becer 2015).

CL represents half of the organic carbon in the biosphere, while HC is the second most abundant biopolymer in nature (Isikgor and Becer 2015). Such amounts highlight the great potential that lignocellulose may have in our future renewable energy matrix. Despite being found in vast quantities, the monomeric saccharide units from the lignocellulose are not readily available for microbial fermentation, and their release is dependent on hydrolysis of the constituting polysaccharides. Since *S. cerevisiae* cannot hydrolyze CL or HC, 2G bioethanol production must be preceded by a chemical/physical pretreatment, followed by chemical or enzymatic hydrolysis (Basso et al. 2013; Isikgor and Becer 2015; dos Santos et al. 2016a).

The initial fractionation of lignocellulose into LG, CL, and HC is achieved by basically four types of pretreatments, such as (1) chemical (acid, alkaline, oxidative delignification, and organosolv), (2) physical (milling, pyrolysis, and microwave), (3) physicochemical (steam explosion, ammonia fiber explosion, and $CO_2$ explosion), and (4) biological (biopulping via fungi, bacteria, and specific enzymes) (Kumar et al. 2009; dos Santos et al. 2016a). Following pretreatment, hydrolysis can be obtained by chemical methods (e.g., dilute or concentrated acid hydrolysis) or enzymatically by cocktails of hydrolases (Basso et al. 2013; dos Santos et al. 2016a). Hydrolysis ensures that CL is broken down into its glucose units, while HC is decomposed into its C5 (xylose and arabinose) and C6 (galactose, mannose, rhamnose, and glucose) monomeric sugars (Palmqvist and Hahn-Hägerdal 2000; Basso et al. 2013; Isikgor and Becer 2015; dos Santos et al. 2016a).

The resulting liquor, referred to as lignocellulosic hydrolysate (LCH), is the actual substrate for downstream fermentations. Unfortunately, along with precious sugars, the hydrolysis also produced many undesirable byproducts toxic to microorganisms. For example, dehydration of xylose and arabinose results in furfural, while 5-hydroxy methylfurfural (HMF) is formed by dehydration of hexoses (glucose, mannose, and galactose) (Palmqvist and Hahn-Hägerdal 2000; Jönsson et al. 2013). Furthermore, furfural can generate formic acid, while HMF can be broken down into formic and levulinic acids. Acetic acid is released upon HC hydrolysis and consists in one of the most abundant inhibitors present in LCHs.

The LG-derived phenolic compounds such as 4-hydroxybenzoic acid, vanillin, catechol, ferulic acid, and coumaric acid, complete the catalog of top-ranking inhibitors. It should be noticed that the full list of LCH inhibitors spreads beyond those cited above, and their identity and concentration in a giving LCH depends on each feedstock used and on the pretreatment method applied (Jönsson et al. 2013). The fermentation efficiency of *S. cerevisiae* in LCHs is heavily compromised by those inhibitors, which cause overall prolongation of lag phases, slower growth rates, reduced BS formation, and decreased bioethanol productivity. Yeast responses to LCH toxicity generally involve ATP and NAD(P)H expending processes to detoxify inhibitors and repair their damage (Piotrowski et al. 2014). For instance, acidification occurs when weak organic acids (chiefly acetic, but also formic and levulinic acids) are generated upon lignocellulose hydrolysis at low pH, weak acids shift to the undissociated form that easily permeates yeast cell membranes. Inside the near-neutral cytosolic pH, acids dissociate and decrease the intracellular pH, triggering the actions of plasma membrane and vacuolar ATPases to clear protons from the cytosol at the expense of ATP hydrolysis (Palmqvist and Hahn-Hägerdal 2000; Jönsson et al. 2013; dos Santos et al. 2016a).

Besides promoting futile waste of energy, decreased intracellular pH further interferes with many enzymatic activities (e.g., glycolytic enzymes) (Palmqvist and Hahn-Hägerdal 2000). On the other hand, the anionic form of weak acids is also toxic by increasing the intracellular osmolarity, which impairs the synthesis of macromolecules and DNA replication, and causes the formation of reactive oxygen species (ROS) (Jung and Kim 2015). In this regard, extreme acetic acid toxicity can lead to programmed cell death (Giannattasio et al. 2013). In compensating manner, yeast cells extrude anionic acids, while lowering intracellular accumulation of several amino acids (Jung and Kim 2015). Generally, acetic acid, with higher $pK_a$ (4.76) and abundance than levulinic and formic acids, champions the toxic effects associated with the organic acids contained in LCHs (Palmqvist and Hahn-Hägerdal 2000; Jönsson et al. 2013; dos Santos et al. 2016a).

As for the inhibitors furfural and HMF, their toxicity is primarily exerted by direct inhibition of enzymes controlling the central carbon and energy metabolism, and by depletion of NAD(P)H pools during detoxification through a cellular pool of oxidoreductase enzymes (Palmqvist and Hahn-Hägerdal 2000; Heer and Sauer 2008; Jönsson et al. 2013; dos Santos et al. 2016a). Such redox reactions may also account for ROS formation as byproducts (Kim and Hahn 2013). Detoxification of furfurals may also occur at the expense of ATP, possibly via their cellular extrusion by efflux pumps (Palmqvist and Hahn-Hägerdal 2000; Jönsson et al. 2013; dos Santos et al. 2016a).

Within the LG-derived inhibitors, higher toxicity has been associated with lower molecular weight phenolic compounds, although the mechanisms of action have not yet been elucidated. In general, the lipophilic nature of phenols accounts for pronounced toxic effects at level of the plasma membrane, although phenols can also cause systemic damages, such as denaturation of proteins, oxidative stress, decrease in intracellular pH, depletion of ATP, translation inhibition, and DNA mutagenesis. Overall, the toxic effects of LCH inhibitors comprise a major obstacle that must be removed to enable cost-effective industrial 2G fermentations. To achieve this goal, many physical and/or chemical treatments, either applied during or after the hydrolysis, have been proposed to minimize the production or to detoxify the inhibitors (Kumar et al. 2009). Similarly, many chemical treatments applied during fermentations have been tested to ameliorate LCH toxicity and/or to improve overall fermentation performance (Jönsson et al. 2013). However, most of these methods demand processes or chemical additives that impact final production costs. A promising alternative is to increase/discover the intrinsic (genetic) capability of *S. cerevisiae* to withstand toxicity of LCH inhibitors.

### 1.6.1 Genetic Advances to Improve Yeast Tolerance to Lignocellulosic Hydrolysates

The advance of knowledge of traits linked to yeast tolerance to LCH inhibitors has mostly benefited from novel approaches such as experimental/adaptive evolution protocols, genome-wide studies, and biology synthetic tools available lately. Adaptive laboratory evolution protocols have been developed followed by genome sequencing, transcriptomic analysis, proteomic and their combinations. In the resulting evolved strains, molecular mechanisms resulting in growth rate improvement under various stress conditions, including LC inhibitors factors were established (Fletcher and Baetz 2020).

As it is known that yeast LHC inhibitors tolerance is a multigenic complex trait (de Witt et al. 2019), advances in systems biology approaches have transformed the way by which cells respond to inhibitor toxicity. Genome-wide approaches have given insight into how yeasts develop tolerance, enabling the identification of genetic and metabolic targets that can be engineered to improve tolerance to fermentation inhibitors as well as revealed optimal yeast genetic backgrounds with insights about how the combination of genes might alter the response towards stresses in the nature.

Prospecting data from transcriptomic studies with *S. cerevisiae* have provided a rational basis for engineering master regulators to elicit global cell responses to toxic LCH inhibitors. For instance, overexpression of the transcription factors (TFs) Msn2 (general stress response) (Sasano et al. 2012) and Yap1 (oxidative stress regulator) (Kim and Hahn 2013), resulted in improved yeast resistance to furfural. Similarly, overexpression of the Haa1 demonstrated systemic adaptation to acetic acid (Swinnen et al. 2017), whereas raised levels of Sfp1 and Ace2 improved fermentation exposed to acetic acid and furfural (Chen et al. 2016a). Besides TFs, higher tolerance to acetic acid and other stresses was also attained through overexpression of global regulators that instead acted at a post-transcriptional (Rtc3) translational (Anb1) (Hasunuma et al. 2016) or even at a post-translational level (Whi2) (Chen et al. 2016b). In contrast, the modifying particular metabolic pathways have been proven by overexpression of genes related to aldehyde reduction (Heer et al. 2009), spermidine synthesis (Kim et al. 2015), and the pentose phosphate pathway (Hasunuma et al. 2014), resulting in higher tolerance to furan aldehydes. Similarly, the resistance to phenolic inhibitors could be improved by synergic expression of heterologous Lcc2 (laccase) and overexpression of endogenous Sso2 (a t-SNARE protein that controls protein traffic to the plasma membrane) (Larsson et al. 2001). Other specific metabolic modifications, such as overexpression of Acetyl-CoA synthetase (Ding et al. 2015a), or the Pep3 protein (required for vacuolar biogenesis) (Ding et al. 2015b), could also enhance yeast tolerance to acetic acid.

Playing with known pathways related to stress regulation also can help to manage the yeast response, such as over or under expressing enzymes. In this regard, it has been reported that glutathione (GSH) intracellular levels can cope with stress responses elicited by toxic compounds found in LCH. It is known that glutathione (GSH) can protect the cell from reactive oxygen species (ROS) and free radicals, and GSH is oxidized to Glutathione disulfide GSSG by reactions with free radicals. Inhibitors present in the LCH, furfural and HMF can act as thiol reactive electrophiles oxidating GSH in *Saccharomyces cerevisiae*. Ouyang et al. (2021) have identified *YMR152W*, a novel aldehyde reductase with catalytic functions for reduction of at least six aldehydes, including two furan aldehydes (furfural and 5-hydroxymethylfurfural), three aliphatic aldehydes (acetaldehyde, glycolaldehyde, and 3-methylbutanal), and an aromatic aldehyde (benzaldehyde) with NADH or NADPH as the cofactor. The *S. cerevisiae* Ymr152wp was classified as the quinone oxidoreductase and is promising for detoxification of aldehyde inhibitors derived from LC hydrolysis. In this sense, if the levels of GSH through overexpressing enzymes on its biosynthetic pathway (GSH1 and GLR1) are increased, then occurs an increasing on *S. cerevisiae* tolerance related to LCH furfural and HMF (Kim and Hahn 2013). Raghavendran et al. (2020) described that native Gsh1p enzyme have regulation by negative feedback and has a threshold because of the inhibition, however, they overexpressed two bacterial enzymes that lacks this kind of regulation, *StgshF* from *Streptococcus thermophilus* and *LmgshF* from *Listeria monocytogenes* which show increasing the glutathione (GSH) content in yeasts confers tolerance towards lignocellulose inhibitors. Subsequently increasing the bioethanol titers.

Another tool available is the use of yeast deletion mutant library (reviewed by Giaever and Nislow 2014), that comprise more than 21,000 mutant strains that carry precise start-to-stop deletions of approximately 6000 open reading frames. This collection includes heterozygous and homozygous diploids, and haploids of both *MAT*a and *MAT*α mating types. The researchers applied yeast deletion mutant library in an agar-based array screening using sub-lethal concentrations of the compound (s) being tested (LCH, mostly phenolics compounds) the researchers were able to find correspondence with tolerance with specific compounds and identified several targets. One example of a suppressor gene is *BNA7* which was found to enable yeast growth, when deleted, in media containing ferulic acid (Fletcher et al. 2019). Likewise, several genes clustered into biological processes related to tolerance over ferulic acid and vanillin were found mainly when these genes are associated with protein transport (COG6, COG7, and ARL1), and chromatin modification and transcription (SWC3, ARP6, YAF9, HTZ1) (Endo et al. 2008; Fletcher et al. 2019). This information helps as scaffold to created possible metabolic engineering on those pathways. Other genes were found using this deletion libraries, using wheat straw hydrolysate and synthetic miscanthus hydrolysate tolerance, were genes involved in oxidative stress response (SOD1, SOD2), protein synthesis (RPL13B, RPL13A) and ergosterol biosynthesis (ERG2) (Skerker et al. 2013; Pereira et al. 2014).

Using adaptive laboratory evolution followed by whole-genome sequencing technologies is possible to access evolution in “real time.” Evolution process by natural selection stablishes that microorganism propagation is under a given selective pressure, which drives towards adapted phenotypes (Dragosits and Mattanovich 2013). The mentioned selective pressure (also known as stress) ensures that adapted genotypes with beneficial mutations outcompete with non-adapted cells in a determined population. These will finally dominate the entire culture after prolonged cultivation A mutant allele can be tested by reverse engineered into the parental (progenitor) background, and may (or not) partially recapitulate the adaptive phenotype gained during the evolution experiment (Barrick and Lenski 2013). Under this perspective, adaptive evolution experiments are excellent in pointing out candidate alleles for metabolic engineering of industrial yeast strains.

There are few experiments so far, mostly using one or two inhibitors isolated for LHC tolerance. For example, the zinc finger transcription factor, *YRR1* acquired a frameshift mutation resulting in a loss of function which improved yeast growth in vanillin (Wang et al. 2017b). In another experiment, nonsense mutations acquired by *MUK1* and *MRS4* resulted in tolerance to coniferyl aldehyde (Hacısalihoğlu et al. 2019).

Using genome shuffling, a technique that is based on performing mutagenesis or followed by adaptive evolution experiment on haploid yeasts of both mating types (a and α), selecting for desirable stress factor in tolerant haploids and mating them to obtain diploid strains (Fletcher and Baetz 2020). Genes including *NRG1, GSH1*, and *GDH1* were identified as important by yeast for improved tolerance to LCH (Biot-Pelletier et al. 2018), this approach allowed to discovery of positive epistasis and the accumulation of beneficial mutations. Cheng et al. (2015) described that, using genome shuffling after adaptive evolution experiments, they re-sequenced several of these adaptive mutants after genome shuffling and identified a total of eight intergenic mutations and nine non-synonymous single nucleotide polymorphisms (SNPs) in coding regions. The main mutation found was *SMF1*, as different alleles in four recombinants. *SMF1* is known to be involved in transport of divalent ions.

Quantitative trait loci (QTL) mapping is another technique that can be used to select traits from promising backgrounds (wild or industrial), especially when the response is multigenic. Using whole-genome sequencing on F1 + n segregating population, originated from crosses of stress-tolerant versus stress-sensible haploids, allows a genome-wide scanning for DNA variations (SNPs/InDels) that correlate with the tolerance phenotype (Meijnen et al. 2016). A statistically significant co-segregation of a given DNA variant with a stress-tolerance trait indicates that both are genetic linked and hence co-localized at a chromosomic level. Thereby, QTL candidates can be observed at a chromosomal location nearby the scored DNA variant. Chosen QTL candidates are then validated if their genetic introduction into the stress-sensible parental strain can recapitulate part of the phenotype associated with the stress-tolerant parental (Pais et al. 2014; Meijnen et al. 2016). Studies related to the QTL mapping of F1 segregants identified an acetic acid-adaptive allele related to the *HAA1* gene, and further analysis of F7 segregants allowed isolation of novel causal alleles of the genes *GLO1, DOT5, CUP2*, and confirm the previously identified allele of *VMA7* (Meijnen et al. 2016).

Synthetic biology is emerging as a cutting-edge tool, especially after the discovery of gene editing technologies, ultimately by CRISPR/Cas technologies. The CRISPR-based knock-out, interference and activation systems have offering genetic screens with broader phenotypic scope (Gutmann et al. 2021) and might unveiled genotype–phenotype relations via precise transcriptional repression. Gutmann et al. (2021) tested yeast growth in the presence of lignocellulose hydrolysate and a supplementing inhibitor cocktail with a plasmid-based CRISPRi system that allows for continuous expression of a nuclease-deactivated (d)Cas9 protein fused to the potent Mxi1 repressor domain, and gRNA's inducible by anhydrotetracycline. They build a library of 1573 gRNAs (up to 6 gRNA locations per gene target) to repress 161 transcription factors and 129 protein kinases, which are highly involved in the regulation of growth adaptation and cellular signaling. They measured, fitness under stress (LCH plus cocktail), competition assays, bioethanol production and confirmed their results using Chromatin Immuno-Precipitation on chip (ChIP-chip) data. They found that hydrolysate-stress adaptation is related to modulation of oxidative (Yap1, Stb5), osmotic (Hog1, Pbs2, Sko1), acidic (Haa1), and general stress (Dot6, Ume6), and show the CRIPRi may identify genetic elements underlying complex environmental conditions encountered by cells in industrial bioprocesses.

## 1.7 Concluding Remarks

The use of 2G bioethanol is worthwhile once might produces biofuels and other biomaterials from sources before neglected or used as burning material. The use of biomass components in a biorefinery is a universal desire, contributing to the feasibility of the process improvement with diversification of the products generated. Studies on yeast copying with stresses from LCH open a wide way in order to understand the steps that will have to take to advance on the knowledge and strategies in this issue. Many approaches had been developed and used in this sense, and with those new technologies, mining genes and metabolic engineering of the desirable traits, together with better LCH ways to produce a less toxic hydrolysate. Biorefinery of biomass is contributing with the environment, decreasing GHG emissions and in a sustainable way producing energy and value-added products.

**Acknowledgments** The authors acknowledge the São Paulo Research Foundation (FAPESP) for the financial support (process number 2019/12997-6; 2017/22401-8 and 2017/24453-5).

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# 2

# Sustainable Biorefinery Processing for Hemicellulose Fractionation and Bio-based Products in a Circular Bioeconomy

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## Abstract

The processing and valorization of hemicellulose fraction biomass from lignocellulosic material, it is an important alternative in these days for the production of high added value compounds and bioenergy in terms of biorefinery philosophy and impacting the development of the circular bioeconomy. For this reason, the development of processes at pilot and industrial level for the fractionation of biomass, and the products applied to the food, materials, and energy sectors are a viable and sustainable alternative for in the development of our society. Therefore, in this chapter, a review on the valorization of hemicellulose fraction, processing technology as hydrothermal processes in batch for extraction of hemicellulose, and high added value products as xylooligosaccharides, xylitol, ethanol and films, coatings, and furans are presented and reviewed.

## Keywords

Biorefineries · Autohydrolysis · Hemicellulose · Severity factor · Lignocellulosic material · Xylooligosaccharides · Pretreatment · Biomass · Oligomers · Liquid hot water · Bioethanol · High added value · Biofuels · Steam explosion

## 2.1 Introduction

The sustainability philosophy in recent years has been of great importance and has attracted attention in the sectors of industry, society, and in public policies in many countries. According to Moldavska and Welo (2017), the sustainability philosophy is an environmental initiative, then leads to the development alternatives and processes to reduce the use of existing natural resources and their preservation on our planet, without putting future generations at risk. Therefore, the sustainability of processes must be compromised by the nexus and use between food, environment and energy (Suarez and Meneghetti 2020). On the other hand, the circular bioeconomy concept has been mentioned and discussed in the last few years, which was an initiative by the European Union looking sustainable developments and reduction of greenhouse gases, with the goal of resource efficiency and low carbon economy by 2050 (Mak et al. 2020; Scarlat et al. 2015).

According to the Task 42: Biorefinery in a circular economy of the International Energy Agency, *the circular economy refers to the as an economy that is restorative and regenerative by design, and which aims to keep products, components and materials at their highest utility and value at all times, distinguishing between technical and biological-cycles. The "Circular Economy" mainly focuses on the efficient use of finite resources and ensures that these resources are re-used as long as possible* (https://www.ieabioenergy.com/blog/task/biorefining-sustainable-processing-of-biomass-into-a-spectrum-of-marketable-biobased-products-and-bioenergy/). Motola et al. (2018) reported different definitions of "bioeconomy" some European countries and they mentioned. The bioeconomy is emphasized in the economic activities, production and processing of bio-based renewable resources as raw material in order to provide bio-based products, processes, and services in all economic sectors in sustainable terms (https://www.ieabioenergy.com/wp-content/uploads/2018/12/Bioeconomy-and-Biorefining-Strategies_Final-Report_DEC2018.pdf). Moreover, several authors have defined the concept of a circular bioeconomy, Mak et al. (2020) and Lara-Flores et al. (2018) defined this concept as the overlap between the concepts of circular economy and bioeconomy, which is based on improving the use of natural resources by reducing greenhouse gases and enhancing waste streams. Stegmann et al. (2020) cited the definition of the European Commission as the production of renewable sources (*raw material*: agricultural residues—forestry residues [lignocellulosic biomass], algal biomass and food-organic waste), and the conversion of these raw materials and waste streams into high added value compounds or products (food, feed, bio-based products, and bioenergy).

On the other hand, the biorefinery concept is an important alternative in the development of sustainability bioprocesses for the production of biobased products (high added value compounds), and biofuels from various biomass feedstocks, this philosophy it is similar to petroleum refinery (Ruiz et al. 2013a, b, 2017, 2020; Pino et al. 2019). The concept of biorefinery should take into account the bioprocess sustainability of the development of the bioeconomy (Aguirre-Fierro et al. 2019; Pino et al. 2020). According to Nizami et al. (2017) the biorefineries are way to achieve sustainable biomass management, having economic and environmental benefits. The biorefineries can be classified as first (crops as corn, sugar cane), second (residues, agroindustrial residues—lignocellulosic biomass), and third generation (algae: macro–micro, as feedstocks), depending on the type of biomass (Moncada et al. 2014; Siller-Sánchez et al. 2018; Velazquez-Lucio et al. 2018; Lara et al. 2020; Aparicio et al. 2020). This section is focused on biochemical platform biorefineries of second generation and bioprocessing design. The biochemical platform biorefinery uses the sugars from biomass into the conversion of high added value compounds and biofuels. The most typical process for obtaining sugars includes different stages as: (1) feedstock; (2) milling; (3) pretreatment; (4) saccharification; (5) fermentation; and (6) product recovery in downstream processes (Ruiz et al. 2012a; Takkellapati et al. 2018; Aguilar et al. 2018a, b).

(1) *Feedstock*: The biomasses have different metabolites—primary (polysaccharides) and secondary (waxes, oils). For second generation of biorefineries, the raw material (residues, agroindustrial residues—lignocellulosic materials) mainly contains cellulose, hemicellulose, and lignin (Moncada et al. 2016). (2) *Milling*: The size reduction stage of biomass is necessary before the pretreatment processing. The main advantages of this operation are: (a) unoccupied volume reduction; (b) subsequent processing stage and easy operational handling in the whole process; (c) increases bulk density and flow properties; (d) improves surface area for the pretreatment stage and the disadvantages are usually related to the operational costs and energy consumption (Ruiz et al. 2011a). (3) *Pretreatment (biomass fractionation or processing)*: This stage is essential for the fractionation of cellulose, hemicellulose, and lignin, and recalcitrance of lignocellulose biomass. This process facilitates the subsequent enzymatic hydrolysis

of cellulose and/or hemicellulose for the production of fermentable sugars. There are many types of pretreatment for biomass that have been developed including physical, physicochemical, chemical, and biological processes. The pretreatment process plays an important role in the biorefinery concept for the production of added-value compounds and biofuels (Ruiz et al. 2011b, 2012b: Aguilar-Reynosa et al. 2017a, b). (4) *Enzymatic hydrolysis*: Enzymatic hydrolysis (saccharification) of cellulose and/or hemicellulose is a heterogeneous reaction process system in which cellulases and/or hemicellulases hydrolyze the polysaccharides into fermentable sugars (glucose, xylose, etc.). This kind of hydrolysis can be considered an environmentally friendly process. Moreover, the enzymatic hydrolysis does not produce inhibitory compounds for the fermentation stage (Pino et al. 2018; Singh et al. 2019). (5) *Fermentation technology*: Process using fermenting microorganisms to convert fermentable sugars to high value-added products and biofuels through submerged or solid fermentation (Ruiz et al. 2012c; Olguin-Maciel et al. 2020; Rosero-Chasoy et al. 2021). (6) *Downstream processes*: In this stage the products are recovery and purified.

The main high added value compounds, fine chemicals from second-generation biorefinery using biochemical platform are: amino acids, enzymes, organic acids, vitamins, antibiotics, xanthan, succinic acid, itaconic acid, adipic acid, 3-hydroxypropionic acid, isoprene, glutamic acid, aspartic acid, sorbitol, furfural, xylooligosaccharides, hydroxymethylfurfural, levulinic acid, glucaric acid, xylitol, and biofuels as bioethanol, biogas, bio-butanol, bio-hydrogen (IEA 2012). Also, Ubando et al. (2020) mentioned that the biorefinery acts as an important strategy in the implementation of circular bioeconomy, Popp et al. (2021) reported that more than 50 countries are experimenting and developing strategies in the concept of bioeconomy and they concluded that the biomass and Chandel et al. (2020) and Kircher (2021) mentioned that the integrated biorefineries industries should play an important role in the value chain in the bioeconomy sector, especially the raw material (biomass) processing. Figure 2.1 shows the scheme of the concept of a circular bioeconomy using biomass as raw material and the integrated biorefinery processing as strategy in the implementation of circular bioeconomy. Since the sustainable biorefinery from lignocellulosic biomass has been reported as a potential strategy to convert this raw material into bio-based products and biofuels, the conversion of hemicellulosic fraction in terms of circular bioeconomy is discussed in this chapter.

## 2.2 Processing and Fractionation of Biomass: Hydrothermal-High Pressure Pretreatment

Hydrothermal pretreatment (autohydrolysis, autocatalyzed hydrolysis, steam explosion, liquid hot water, hot compressed water) for biomass is one of the most promising processes to be applied from laboratory-pilot-demonstration to industrial scale. In this process, only liquid phase water or steam is used (Ruiz et al. 2013a, b, 2017, 2020; Ruiz 2017). Typical operating conditions for this process are

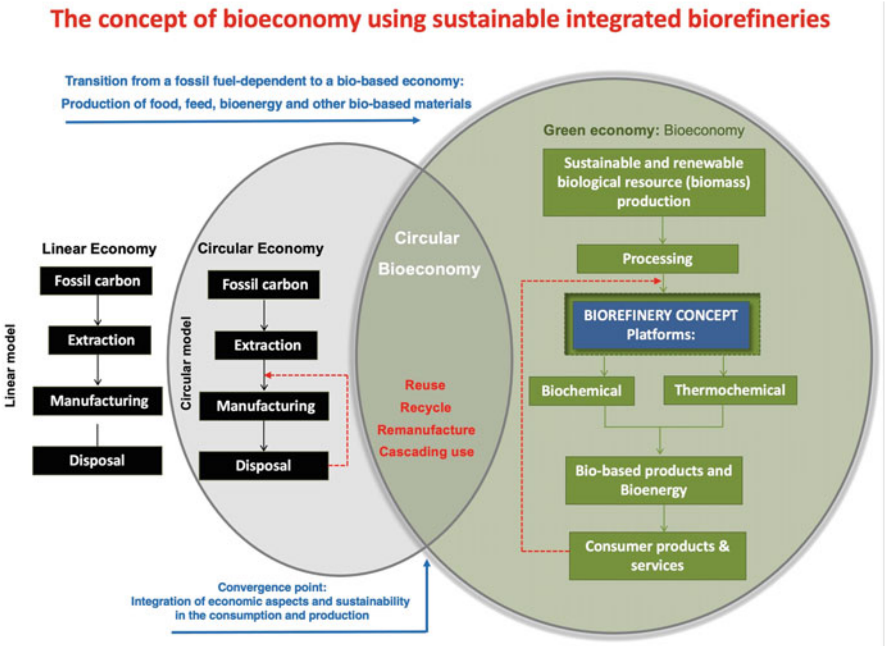

**Fig. 2.1** Scheme of the concept of a circular bioeconomy using biomass as raw material and the integrated biorefinery processing

temperature (150–220 °C) and pressure (71–285 psi) and the correlation of these variables can be represented by the severity factor [log ($R_o$)] (Overend et al. 1987; Aguilar-Reynosa et al. 2017a, b; Aguilar et al. 2018a, b; Chornet and Overend 2017). During this process the biomass is fractionated, recovering the hemicellulosic fraction in the liquid fraction and cellulose + lignin in the solid fraction, being this process very selective for the solubilization and depolymerization of hemicellulose into high/low-molecular weight xylo-oligomers, xylose, and furfural. The hydrolysis process in hydrothermal pretreatments is possible due to the autoionization of water (hydronium ions) and acetic acid from the acetyl groups of hemicellulose (Ruiz et al. 2013b). This type of pretreatment has recently been reviewed by Ruiz et al. (2020). Ruiz et al. (2020) reported the engineering aspects in the development of the hydrothermal process to pilot scale operation, these types of processes can currently be operated in batch or continuous mode, being one of the great advantages in the pretreatment stage for lignocellulosic biomass. Figure 2.2a shows the tubular hydrothermal pilot reactor in the Biorefinery Pilot Plant at Autonomous University of Coahuila (https://biorefinerygroup.com/) for biomass fractionation in liquid phase (hemicellulosic fraction) and solid phase (cellulose + lignin fraction) operated in batch mode. Figure 2.2b shows the automatic process control panel of the tubular hydrothermal pilot reactor.

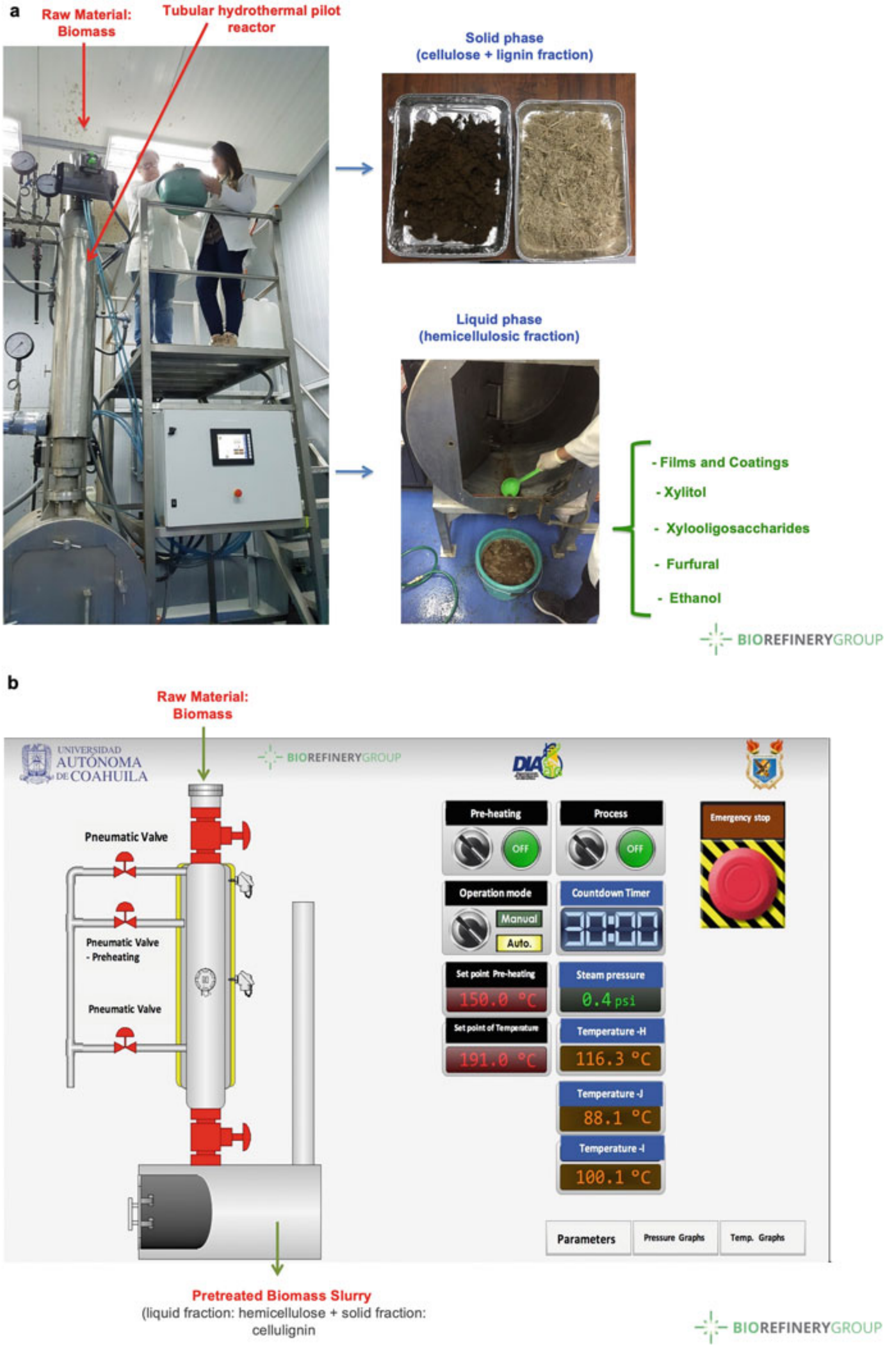

**Fig. 2.2** (**a**) Tubular hydrothermal pilot reactor; (**b**) scheme of automatic process control panel of the tubular hydrothermal pilot reactor

In the following sections, the most promising high added value products (films and coatings, xylitol, xylooligosaccharides, furfural and its derivatives, and ethanol) in the circular bioeconomy concept from the hemicellulose fraction are reported and discussed.

## 2.3 High Added Value Products from Hemicellulosic Fraction

### 2.3.1 Films and Coatings

Hemicelluloses present very interesting properties that guarantee that they can be used in different packaging solutions, such as films and coatings, alone or in combination with other materials. Besides their film-forming capacity, it is biodegradable, presents moderated compatibility with some biopolymers and polymers and depending on the source and extraction method can be considered food grade. Due to these characteristics, hemicelluloses have been widely explored in the last 10 years as a bio-based and biodegradable material for packaging applications.

Hemicelluloses can be used as a coating where the two main approaches are: to be applied directly on a food product to form a thin film protecting the food or as an additional layer in a packaging material and therefore used to improve the properties of the coated packaging material. Moreover, they can also be used as the main material for the production of films or as filler of other film-forming materials. The way that is used is mostly dependent on their physicochemical characteristics that are dependent on their source and extraction method (as mentioned in Sect. 2.2—hydrothermal processing). One of the approaches to increase the versatility of hemicellulose is its chemical modification, where it is possible to change its properties and increase the compatibility with other materials.

Their use as an additional layer in other packaging materials showed to be one of the most interesting applications, with several publications and commercial applications using this strategy to improve the barrier properties of packaging materials, such as plastic and paper. This strategy, using a sustainable coating based on hemicellulose, can improve barrier properties, such as oxygen and water vapor permeabilities, maintaining the compostability or recyclability of the coated materials. One of the commercial examples was presented by an extinct Swedish company, Xylophane. They proposed a method for the production of flexible films or coatings for packaging based on hemicelluloses combined with a cross-linking or hydrophobized agent (Gatenholm et al. 2008). The same company, in 2013, presented the possibility of using hemicelluloses and a nanocomposite (phyllosilicate) for the development of packaging with improved moisture resistance (Gröndahl et al. 2013). Xylophane was acquired by the company Seelution in 2016 (https://seelution.se/).

The use of hemicellulose as coating in paper-based materials has shown to be one of the interesting applications of hemicellulose-based coatings. They can be used to reduce the environmental impact, and the recyclability and compostability problems of the normally used petroleum-based coatings (normally used to improve barrier properties and improve hydrophobicity of paper) (Anthony et al. 2017). In 2014, Kisonen et al. (2014) studied the influence of unmodified and esterified *O*-acetyl galactoglucomannan coatings in carton board properties. They showed that esterified *O*-acetyl galactoglucomannan coatings esters had better water resistance and slightly higher grease barrier values than *O*-acetyl galactoglucomannan (Kisonen et al. 2014). Later, Ramos et al. (2017) showed the possibility of using chemically modified xylan (using the etherification and esterification route) to improve the barrier properties of paper. The esterified xylan coating decreased the water vapor permeability of the paper up to 30-fold and allowed to achieve oxygen transfer rates similar to the values reported for papers coated using polyethylene films (Ramos et al. 2017).

Besides being used as a coating for other packaging materials, they can also be used directly in food products. When applied in food surface, they form a thin layer that acts as a barrier to gases, increasing their shelf-life. In this case, they can also be used as a carrier of active compounds that act preventing the microbiological spoilage of foods or oxidation. The edibility of hemicelluloses is used to guarantee their safety if eaten with the food. In this regard the most used hemicellulose were galactomannans, where they were tested in cheese and fruits, showing the ability to increase shelf-life acting and barrier to gases but also as a way to delivery active compounds in food surface (Cerqueira et al. 2009; Martins et al. 2010; Lima et al. 2010). Also, hemicellulose extracted from hazelnut shells was used to coat dried apricots and showed to be a promising material to be used as a coating during apricots drying (Ubeyitogullari and Cekmecelioglu 2016).

Several works explored the use of hemicelluloses as stand-alone films, using hemicellulose alone or in combination with other materials. They can be used as wrappers, plastic bags, or trays. In 2008, Höije et al. (2008) modified enzymatically hemicelluloses from barley husks for the preparation of high oxygen barrier films or coatings (Höije et al. 2008). In other work, glucuronoxylan was extracted from aspen wood and combined with xylitol and sorbitol for the production of films. Also aiming to improve their barrier properties, Saxena et al. (2011), reinforced xylan films with cellulose nanocrystals (CNCs) obtained from acacia bleached Kraft pulp fibres and softwood Kraft fibres. The results showed that xylan films reinforced with 10% of CNCs (obtained through sulphuric acid treatment) presented the lower water permeability values among all the composite films studied. The addition of nanocelluloses, such as cellulose nanofibers and cellulose nanocrystals, has been explored in the last years (Huang et al. 2017a; Xu et al. 2019a), but other of the options presented and used to improve hemicellulose-based films was the addition of inorganic materials such as graphene oxide (Rao et al. 2019), bentonite nanosheets (Huang et al. 2019), and clay nanoplatelets (Guan et al. 2014).

Hemicelluloses can also be used in blends with other compounds (e.g. other biopolymers, plasticizers, and surfactants) in order to enhance the moisture-barrier properties, strength, stiffness, and flexibility. As a result, hemicelluloses obtained from wheat straw and wheat bran were proposed as bio-based materials for film production through a blend of galactomannan and k-carrageenan, and chitosan, respectively (Costa et al. 2015; Ruiz et al. 2013b). Using a blend of galactomannan and k-carrageenan, results showed that the incorporation of wheat straw hemicellulose extracted by autohydrolysis process can help in decreasing the water vapor permeability and increase the tensile strength of the films (Ruiz et al. 2013b).

In 2015, Chen et al. (2015) combining several approaches, showed the possibility of combining montmorillonite, chitin nanowhiskers and polyvinyl alcohol into quaternized hemicelluloses for the production of films. They showed that the combination of the different materials (fillers and other polymers) resulted in hybrid films with improved barrier and mechanical properties (Chen et al. 2015).

Other of the strategies to improve hemicellulose-based films is the chemical modification as presented in several publications where it has been showed the possibility of using carboxymethylation (Alekhina et al. 2014), periodate oxidation followed by reduction (Kochumalayil et al. 2013), acetylation (Stepan et al. 2012), long-chain anhydride modification (Zhong et al. 2013) and crosslinking (Shao et al. 2019) to change and improve their physicochemical properties. Mugwagwa and Chimphango (2020) evaluated the use of acetylated hemicellulose from wheat straw in combination with nanocellulose and a coating of polycaprolactone for food applications. They evaluated the film's behavior in different food simulants and foresaw the possibility of using the films for fatty foods where the solubility is low. In addition, they added to the films polyphenols that can guarantee active properties to the films (Mugwagwa and Chimphango 2020). Zhang et al. (2020) studied the transesterification of hemicellulose from hardwood pulp with vinyl laurate and their use for film's production. They showed the possibility of producing semi-transparent films by the solvent casting method. They showed that increasing the degree of substitution improved the barrier properties of the films. This low permeability justified the better results obtained for packed green chillies, evaluated during the work, with films based on a hemicellulose-vinyl laurate with a high degree of substitution (Zhang et al. 2020).

One of the important points when considering using hemicellulose as stand-alone film is their industrial production and if the technologies available are easy to adapt for the use of this kind of materials. Therefore, it is necessary to know their behavior under other industrial processing technologies. In this regard, the chemical modification of hemicelluloses can also help the industrialization of these materials, since it can help reaching the requirements needed for the processing. One of the attempts was performed by Farhat et al. (2018) were they evaluated the xylan (from bleached hard wood pulp) chemical modification by ring-opening graft polymerization of ε-caprolactone. They showed that the obtained material present thermoplastic properties that allowed them to be used in the molding process for the production of films. In the end, it was possible to verify that the obtained materials present a good biodegradability (95.3–99.7%) (Farhat et al. 2018).

### 2.3.2 Xylitol

Xylitol is natural five-carbon alcohol ($C_5H_{12}O_5$) found in small amounts in fruits, vegetables, algae, and mushrooms (Mohamad et al. 2015). It is used in the pharmaceutical and food industries as an alternative sweetener, as it is similar to common sugars in sweetness and has low-calorie levels, in addition to other interesting properties such as anti-cariogenic, antioxidant, moisturizer, stabilizer, cryoprotectant, and freezing point reducer (Mohamad et al. 2015; Xu et al. 2019a; Trivedi et al. 2020).

Xylitol is a white granular solid, odorless, crystalline, and very soluble in water. It is considered the sweetest in the polyols class, and with the lowest glycemic index (Arcaño et al. 2020). Among the pentoses, xylitol is one of the most important for the development of integrated processes in biorefineries, due to its economic value and its diverse applications (Pulicharla et al. 2016). Xylitol is used as a diabetic sweetener because it is rapidly absorbed by liver cells and released slowly into the blood, preventing sudden changes caused by sugars such as sucrose and glucose (Arcaño et al. 2020). It is also used in oral health applications, such as chewing gums and toothpaste, as it has a synergistic effect with other agents such as fluoride in preventing cavities (Pulicharla et al. 2016; Arcaño et al. 2020). In addition to applications in other sectors of the industry such as the production of cleaning products, beauty creams, and lotions to maintain moisture (Granström et al. 2007).

In biorefinery platforms based on vegetable biomass, xylitol is considered one of the most important products derived from carbohydrates and can be produced by chemical or biological conversion of hemicellulose present in the biomass structure (Bozell 2008; Xu et al. 2019b). Large-scale conversion of biomass to xylitol is traditionally carried out by chemical routes through the hydrogenation of purified xylose (from the hydrolysis of hemicellulose) using chemical catalysts at high pressure and temperature, increasing process costs (Mohamad et al. 2015; López-Linares et al. 2018). The steps of the chemical route are (a) hydrolysis of biomass to remove lignin and reduce the degree of crystallinity of the structure, (b) purification of the hydrolyzate to obtain pure xylose, (c) hydrogenation of xylose to xylitol, and (d) crystallization xylitol (Mohamad et al. 2015).

Chemical processing can result in the formation of unwanted by-products during catalytic hydrogenation of xylose, requiring upstream purification steps to obtain pure xylose and downstream to remove by-products resulting from the chemical reaction, increasing energy expenditure and economic process (Arcaño et al. 2020). In view of safety and environmental contamination concerns using the chemical reduction of xylose to xylitol, the biotechnological route employing microorganisms and enzymes is being explored by several researchers (Xu et al. 2019b). However, although the conversion yield through biotechnology can be increased by optimized processes and are more secure and environmentally sustainable, the chemical route is still very competitive in terms of industrial scale (Irmak et al. 2017). Thus, recent research using chemical routes for obtaining xylitol seeks to optimize processes with a reduction in the concentration of chemicals and using plant residues with a high hemicellulose content and abundant as raw material, which can be converted into high yield xylitol (Irmak et al. 2017).

The biotechnological conversion of xylose to xylitol by means of microorganisms and/or enzymes is a strategy with a more sustainable bias, of lower economic cost due to the availability of biomass and because the operating conditions are milder, requiring less energy for the process (Mohamad et al. 2015). Different microorganisms have the potential to convert xylose using it as a carbon source and converting it into xylitol, being generally mediated by enzymatic catalysis, the main enzymes involved in this process being xylose reductase and xylitol dehydrogenase (Mathew et al. 2018; Xu et al. 2019b). The biological route for converting xylose to xylitol is carried out by (a) hydrolysis of biomass, (b) detoxification of the hydrolyzate, (c) xylose fermentation to xylitol mediated by microorganisms and/or enzymes, (d) xylitol purification (Mohamad et al. 2015). Among microorganisms, yeasts are preferred for this process due to high rates of pentose assimilation in some species and stable levels of expression of xylose reductase and xylitol dehydrogenase, resulting in high productivity in xylitol (Xu et al. 2019b). *Candida species* are the most reported for use in this xylitol production pathway (de Albuquerque et al. 2014), and efforts are being made in the field of genetic engineering to express interesting genes in the conversion of xylose to xylitol in microorganisms to increase yield (Zhang et al. 2018a).

Currently, the main bottleneck in the production of xylitol refers to the purification processes after obtaining it, due to impurities formed during the obtaining of hemicellulosic biomass that is responsible for the high cost of xylitol on the market (Chandel et al. 2018). With regard to biotechnological bias, the scale expansion process has not yet been established (Arcaño et al. 2020). The recovery of xylitol in vegetable biomass hydrolyzate media is little explored in scientific articles, but it is essential to establish integrated technological solutions for second-generation biorefinery platforms (de Albuquerque et al. 2014).

Xylitol production is expanding, mainly due to the high market demand due to the beneficial characteristics of its use, which increases the need for research that enables high yields in processes that are less economically costly and environmentally sustainable (de Albuquerque et al. 2014). The use of vegetable biomass residues has been widely explored as a potential raw material in the production of xylitol (de Albuquerque et al. 2014). The possibility of using residual biomass for the production of xylitol further increases the interest and adds value to this bioproduct, this is also possible through research that develops a cheaper and more efficient technology for obtaining xylitol in biotechnological pathways, considering the control of parameters and optimization for a desirable yield. This suggests that new processes will be needed to co-produce bioproducts within a biorefinery based on the concept of circular economy (Özüdoğru et al. 2019).

### 2.3.3 Xylooligosaccharides: Production and Market Potential

In recent years, increasing consumer awareness of the diet-wellness relationship has increased the demand for functional foods to improve human health (Hong et al. 2019). Among these, prebiotics are attractive compounds due to their multiple beneficial effects including improvement of mineral absorption and bowel functions, regulation of lipid and glucose metabolism, reduction of the risk of colon cancer, exhibiting immunomodulatory and anti-inflammatory activities, and protection against cardiovascular disease (Dávila et al. 2019; Farias et al. 2019). More recently, prebiotics have also been reported to improve mental disorders such as depression, anxiety, stress, cognitive function, and sleep/wake cycle disruptions (Tabrizi et al. 2019). Due to this myriad of health-promoting effects, prebiotics have been increasingly used in the food industry as functional ingredients for the preparation of different food products including dairy, beverages and health drinks, cereal bar, confectionary, infant formulas, meat products, animal feeds and as supplements (Ashwini et al. 2019; Farias et al. 2019). According to the current analysis of MarketsandMarketsTM, the world market for prebiotics was valued at USD 4.07 billion in 2017, and it is forecasted to reach a value of USD 7.37 billion by 2023, at a CAGR of 10.4% (MarketsandMarketsTM 2018). The prebiotics market is led by Asia-Pacific region including China, India, and Japan with a 9.5% CAGR over the forecast timeline (Amorim et al. 2019a). In European, the prebiotics market is mainly dominated by France, Italy, and Germany and is anticipated to register a lucrative growth at more 9% for the same period (https://www.prnewswire.com/news-releases/prebiotics-market-value-to-surpass-usd-7-2-billion-by-2024-global-market-insights-inc-300916592.html). Many companies are involved in obtaining prebiotics from different raw materials. Some examples of the manufacturers operating in the global prebiotics market are Cargill Inc., Kraft Foods Group, Inc., Abbott Laboratories, Beneo GmbH and Bright Food (Group) Corporation Limited (https://www.grandviewresearch.com/industry-analysis/prebiotics-market).

Nowadays different compounds are commercialized as prebiotics including inulin, lactulose, galactooligosaccharides (GOS) and fructooligosaccharides (FOS), xylooligosaccharides (XOS), and pectic oligosaccharides (Ashwini et al. 2019; Dávila et al. 2019). Among these compounds, XOS have been proposed as a new class of prebiotics that has gained attention because of its additional benefits beyond its prebiotic potential. XOS present a moderate degree of sweetness, stability of pH and temperature, acceptable organoleptic properties and they do not exhibit toxicity or negative effects on human health (Amorim et al. 2019b; Mano et al. 2018). All these characteristics make XOS suitable compounds to be incorporated into several foodstuffs (Gullón et al. 2018).

The valorization of lignocellulosic by-products through the production of XOS is an interesting strategy since it responds to the current issue of waste disposal and satisfies consumer demand for functional food from natural sources (Poletto et al. 2020). XOS are mixtures of oligosaccharides with a branched structure composed of 2–10 xylose units linked through β-(1→4)-bonds containing a diversity of substituents, namely acetyl groups, uronic acids, and arabinose residues (Álvarez et al. 2017; Amorim et al. 2019a). In the past few years, XOS have been obtained from a number of biomass sources, including hardwoods (Gallina et al. 2018), sugarcane bagasse (Bian et al. 2014), vine shoots (Dávila et al. 2016), corncob (Boonchuay et al. 2018), rye straw (Gullón et al. 2010), peanut shells (Rico et al. 2018), among others, using chemical, hydrothermal, and/or enzymatic methods (Dávila et al. 2016; Hong et al. 2019). Chemical or hydrothermal processes present some problems such as use of noxious chemicals, the formation of unwanted compounds (hydroxymethylfurfural and furfural), low control of the degree of polymerization of the oligosaccharides formed (Álvarez et al. 2017; Amorim et al. 2019b; Rico et al. 2018), and high costs associated with the downstream process (Bian et al. 2014). The use of enzymes is a more environment-friendly strategy since it does not use noxious chemicals and allows to control over DP of the produced oligosaccharides. The production of XOS is generally done in two stages: a first chemical or hydrothermal pretreatment in order to solubilize the xylan of the lignocellulosic material followed by xylan hydrolysis by xylanolytic enzymes (Arai et al. 2019; Huang et al. 2017b). This strategy has been evaluated by Álvarez et al. (2017) that described a process based on steam explosion pretreatment to extract the xylan from wheat straw followed by endo-xylanase hydrolysis to produce XOS with a DP2-DP6. In another study, Dávila et al. (2019) only applied one stage of hydrothermal treatment to obtain oligosaccharides from vine shoots. According to the authors, XOS exhibited a high range of DP varying from 2 to 17.

XOS production based on these processes is so far expensive mainly due to the low yields obtained in the pretreatment stage and the high costs of the enzymes (Amorim et al. 2019a). However, recent advances in production methods will favor obtaining XOS more efficiently, making the process economically feasible, which in turn will drive the market for these compounds. In this sense, the XOS market is expected to reach 130 million US$ by 2023 (Amorim et al. 2019a). Currently, there are two major XOS manufacturers that have received GRAS certification for its use in a variety of food categories: Shangdong Longlive Biotechnology (China) and Prenexus Health (USA) that produce XOS from corncob and sugarcane fiber, respectively (Poletto et al. 2020).

As previously mentioned, XOS have remarkable potential as food ingredients due to their physicochemical properties and multi-dimensional effects on human health. Several prebiotic oligosaccharides, especially FOS and inulin have been extensively used in various food formulations, however, the incorporation of XOS has been poorly reported for this purpose. For example, Ferrão et al. (2018) assessed the effect of the addition of XOS as a fat substitute and prebiotic agent in a typical Brazilian processed cream cheese. According to their results, the incorporation of 3.3% of XOS enhanced physicochemical and rheological characteristics, increasing apparent viscosity, elasticity, and firmness. The authors concluded that XOS could be used for the development of healthy and low-fat processed cheeses.

Ayyappan et al. (2016) studied the effect of the addition of XOS at three different levels (5, 10, and 15%) on the nutritive value, physicochemical properties, moisture, color, texture, and storage stability. The results indicated that dietary fiber content in enriched cookies increased in a dose-dependent manner. Cookies formulated with 5% XOS resulted in a more stable product during storage at 25 °C for 21 days. In addition, enriched cookies retained 74% of the added XOS, suggesting the prebiotic functionality of the product.

Recently, Souza et al. (2019) also tested the impact of the addition of XOS (1.25 g/100 mL) on the quality parameters of strawberry-flavored whey beverage. The findings demonstrated that XOS incorporation improves functional characteristics, namely antioxidant activity, ACE inhibitory activity, and α-amylase and α-glucosidase inhibition. Besides, the rheological properties are also modified, observing an increase in viscosity that is attributed to the formation of a strong network between the XOS and the protein through hydrogen bonds or due to the increased water retention capacity of these compounds.

XOS were also evaluated for their interesting technological properties. For example, Zhang et al. (2018b) demonstrated the cryoprotectant effect of XOS on peeled whiteleg shrimp. The results revealed that soaking in XOS solutions before frozen storage reduced losses during thawing and cooking compared to the control (freshwater treatment). Computational studies carried out attributed this cryoprotective effect to the formation of hydrogen bonds between the XOS and the polar residues of the proteins of shrimp muscle and by decreased water mobility that limits the growth of ice crystals.

### 2.3.4 Furfural and Its Derivatives

The obtention of value-added chemicals, fuels, and energy using renewable resources of lignocellulosic nature following the biorefinery concept has increased in the last decades at global level as a potential solution on the one hand due to the depletion of fossil sources and on the other hand to mitigate the environmental problems (Rachamontree et al. 2020).

In this context, several building blocks with high potential industrial applications in the future can be produced from lignocellulosic materials. 2-Furaldehyde (furfural), a furanic compound is obtained from polysaccharides rich in pentoses such as xylans, mannans, xyloglucans, and β-glucans (Delbecq et al. 2018). The research on the bio-based production of furfural in the last years has been encouraged by the current trend toward a sustainable development model that has boosted the bioeconomy and circular economy. Precisely, this furan derivative can be produced from the hemicellulosic fraction of lignocellulosic rich in pentose (Guo et al. 2019) and it is a green platform chemical that can be used as precursor in the obtention of several compounds as antacids, fertilizers and moreover, it is widely applied in refining oil, plastic production, pharmaceutical and agrochemical industries (Machado et al. 2016). Therefore, furfural and its derivatives can be considered as alternative raw materials to replace the fossil fuels (Rachamontree et al. 2020).

Furfural is mainly produced by an acid hydrolysis of hemicelluloses present in lignocellulosic biomass to obtain xylose, which is subjected to an acid-catalyzed dehydration to produce furfural. This compound has been recognized by the US Department of Energy (DOE) as one of the top 12 value-added chemicals obtained from biomass, with a world market of 300,000 tons per year (Morais et al. 2020).

The industrial production of furfural dates from 1921 and it was based on the Quaker Oats batch process employing oat hulls. However, the furfural yield of this process was below 50% and had high energic requirements and harmful environmental consequences. To achieve highest furfural yields, Quaker Oats developed a continuous process with a 55% of yield but this system continued being expensive (Morais et al. 2020). According to Morais et al. (2020), until now the highest yield informed for the furfural production is 83% and it involves the use of pentosans and an additional recovery stage. Nowadays, agroindustrial and forestal biomasses rich in hemicelluloses and generated in huge amounts annually are the major raw materials used for the obtaining of furfural (Machado et al. 2016). The main challenge in the production of furfural is the development of profitable and sustainable processes boosting an intense research in this field over the years (Morais et al. 2020). Moreover, another key point is to avoid the degradation of furfural by secondary reactions that take place during its synthesis (Karinen et al. 2011).

The strategies collected in the literature to produce furfural from hemicellulosic sugars encompass its synthesis without catalysts such as dehydration in critical solvents and dehydration using hot water pretreatment, synthesis using homogeneous catalysts such as dehydration in the presence of mineral acids, organic acids, and metal salts, use of ionic liquids, by catalysis with solid acids such as carbon acids, oxides, phosphates, silicates, among other (Delbecq et al. 2018). Other processes proved in the last decade are based on the combination of biphasic systems with emerging technologies. Each one of these processes has advantages and inconveniences and parameters such as catalysts, solvents, equipment, and technology involved in them could be optimized for the bio-based furfural production (Delbecq et al. 2018).

The global market for furfural is expected to reach USD 1200.9 million (652.5 ktons) by 2020, growing at a CAGR of 11.9% from 2014 to 2020, according to a new study by Grand View Research, Inc. (https://www.grandviewresearch.com/press-release/global-furfural-market). As mentioned above, furfural is a platform chemical that allows to synthesize a wide range of chemical compounds. Almost 100 chemicals can be directly or indirectly obtained from furfural; actually, furfuryl alcohol, tetrahydrofuran, maleic anhydride, 2-methyltetrahydrofuran, and 1,5-pentanediol are the main furan-derivatives produced on a commercial scale (Xu et al. 2020), which is also expected to have a positive influence on the market growth. Taking into account the information collected above, novel greener processes should be developed that address the major yield limits of furfural production because this platform chemical is outlined as a promising precursor of other compounds obtained usually from fossil resources. The approach based on the use of C5 hemicellulosic sugars from lignocellulosic materials following the biorefinery concept to obtain furfural seems a suitable alternative to the conventional methods. Moreover, the production of furfural as part of a lignocellulosic biorefinery would allow a more profitable process and contribute to establish a circular bioeconomy.

### 2.3.5 Ethanol from Hemicelluloses: Fermentation of Hexoses and Pentoses

The replacement of fossil fuels by biofuels, motivated by problems related to the production chain and the release of harmful gases into the atmosphere is a necessity nowadays (Yilmaz and Atmanli 2017; Tayeh et al. 2020; Ubando et al. 2020). In addition to the environmental problems caused by the use of fossil fuels, the growth in world demand for energy has led to an increase in consumption of fuels. Thus, the search for new energy matrices is a way to minimize these impacts (Lin et al. 2012; Yilmaz and Atmanli 2017; Martins et al. 2018). The production of bioethanol from renewable sources has been gaining ground over the last few years, being the biofuels produced mainly by crops such as sugar cane and corn starch. However, the production from lignocellulosic agricultural residues has been achieving important advances in their conversion routes, such as pretreatment optimization, conversion of sugars with lower molecular weight, and use of more efficient microorganisms in the fermentation of all types of sugars from biomass (Martins et al. 2018; Mishra and Ghosh 2020).

Vegetable biomass and industrial residues stand out for being low cost and renewable sources, available in large quantities (Saha et al. 2015; Phitsuwan et al. 2016). Plant biomass is composed of cellulose, glucose, hemicelluloses, and heteropolymers containing xyloses and lignin (Kumar et al. 2018; Arevalo-Gallegos et al. 2017). The most abundant fraction in these vegetable biomasses is cellulose, followed by hemicellulose, which consists of pentoses and hexoses. A variation can be observed in the biomass source, according to the sugar units that are commonly present in hemicellulose, which can be xyloses, arabinoses, glucose, mannose, glucuronic, and galacturonic acids (Kumar et al. 2018; Habib et al. 2017).

Biomass can be resistant to degradation processes by chemical or enzymatic methods, and these steps are necessary for the transformation of their polysaccharides into simple monomers for later fermentation and obtaining bioethanol (Isikgora and Becer 2015). This high resistance generates a series of bottlenecks in the production chain, which may make production more difficult, due to the need of pretreatments under adverse conditions of temperature and pressure, as well as highly selective microorganisms to carry out the fermentation. Therefore, the challenges are: the search for pretreatments in milder conditions; the use of genetically modified strains; or the selection of suitable strains from the environment, seeking the optimization of the upstream of the bioprocesses making them more aligned with the concepts of biorefinery and circular bioeconomy (Ko et al. 2016; Ubando et al. 2020; Tayeh et al. 2020). Figure 2.3 shows the processes for obtaining bioethanol from lignocellulosic biomass. Furthermore, it presents some strategies that are being developed in each part of the production process to add value to this production chain, bringing greater yields and making the processes more bioeconomic.

In the circular bioeconomy, the main objective is the effective valuation of biomass, using all its fractions, seeking the generation of products with high added value and the reduction of the generation of waste or undesirable products. This concept is in line with the concept of integrated biorefineries (D'Amato et al. 2017). Each process for obtaining biofuel from various raw materials must be studied to reduce processes and costs, as well as to improve technologies for obtaining products from unused fractions (Kumar et al. 2018; Ubando et al. 2020; Tayeh et al. 2020). Many stages of the processes for obtaining bioethanol are elucidated, through pretreatments to achieve greater digestibility of cellulose providing greater enzymatic accessibility for more efficient obtaining of fermentable sugars (Zabed et al. 2016; Smullen et al. 2019; Kumar et al. 2020).

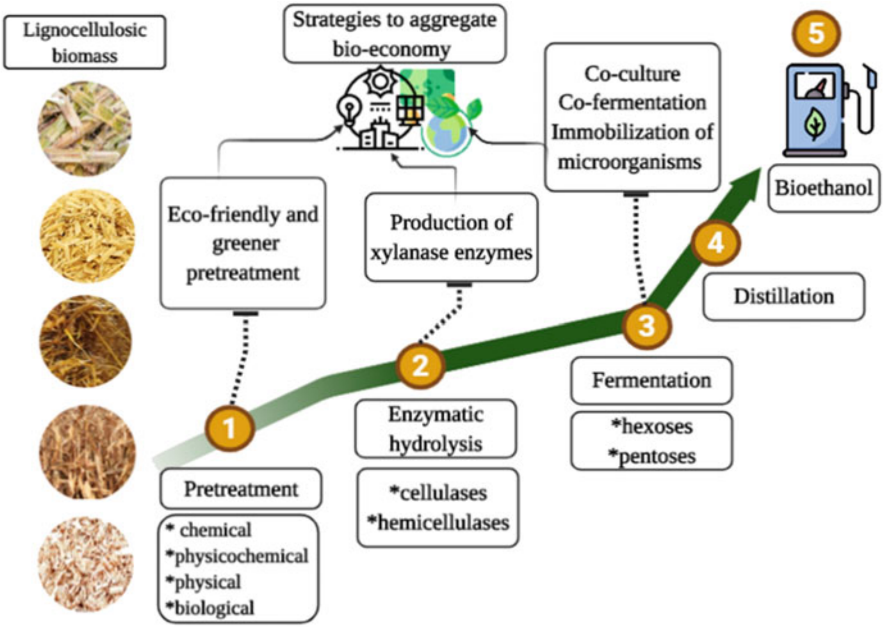

**Fig. 2.3** Processes for bioethanol production from lignocellulosic biomass from pentoses and hexoses

In general, to obtain access to these fermentable sugars, pretreatments are necessary, which are carried out using diluted acids and bases or high vapor pressure (Jahnavi et al. 2017). With the effective action of these pretreatments, the structure of lignin and hemicelluloses are disrupted, and their fractions can be transformed into different monomers. However, the accomplishment of these pretreatments in more adverse conditions can result in the formation of by-products, demanding high use of energy and water, which triggers discussions regarding the sustainability (Liew et al. 2014; Ko et al. 2020). As much as they are efficient in structural rupture, these steps can interfere with subsequent hydrolysis and fermentation processes (Bauli et al. 2019).

Recent studies, seeking high structural rupture efficiencies and lower generation of by-products are being carried out using solvents, including ionic liquids (Szalaty et al. 2018; Garlapati et al. 2020), which show good release efficiencies and milder operational conditions. The use of ionic liquids has been gaining space due to their high availability and biodegradability when used in lignocellulosic materials, performing reactions of acetylation, benzoylation, and carbonylation of biomasses, transforming them into molecules of lower molecular weight (Szalaty et al. 2018), enriching the use of these raw materials and being able to consolidate their use within the biorefinery concepts.

Vegetable raw materials can have a percentage of hemicellulose ranging from 20 to 35%, and hydrolysis can generate hexoses and pentoses (Kuhad et al. 2011;

Kumar et al. 2018). While hexoses are monosaccharides such as glucose, galactose, and fructose that are widely assimilable as a source of substrate for fermentative anaerobic microorganisms, pentoses are monosaccharides such as xylose and arabinose, normally not usable by strains of Saccharomyces cerevisiae. Thus, pentoses are inhibitors in fermentation by *S. cerevisiae*, reducing the final ethanol yield (Paulova et al. 2015; Li et al. 2017; Liu et al. 2019; Roque et al. 2019).

In addition to the obstacle related to the degradation resistance of the lignocellulosic structures, the inhibitors generated during the fermentative processes can impair the entire productive chain. During the transformation of hexoses into ethanol the generation of metabolites such as acetic acid may also occur. In these cases, the inhibitors from the raw materials do not significantly interfere in the efficiency of the processes (Li et al. 2017; Hans et al. 2019).

The main inhibitors generated during pentose fermentation that negatively influence fermentation efficiency are phenol, vanillin, syringaldehyde, furfural, formic acid, and levulinic acid (Li et al. 2017). Among the processes already developed to solve the pentose problem, the use of genetically modified microorganisms (mainly fungi and bacteria) is capable to produce specific enzymes or even carry out the simultaneous fermentation of hexoses and pentoses. Another possibility is the separation of the pentoses from the fermentation medium after hydrolysis. The hexoses follow the standard fermentation processes and the pentoses are transformed into products with high added value such as bio-butanol, bio-hydrogen, biopolymer, 2,3-butanediol, 1,3-propanediol, organic acids, xylitol, and furfural (Kuhad et al. 2011; Kumar et al. 2018; Dai et al. 2020).

Co-fermentation and co-culture are examples of processes that arise to solve the problem involving the simultaneous fermentation of pentoses and hexoses. The co-fermentation process uses microorganisms capable of acting on hexoses and pentoses, in addition to metabolizing these sugar sources. Furthermore, these microorganisms are tolerable to the presence of inhibitors.

Co-culture processes are carried out through the use of different strains of microorganisms in the same fermentation system, seeking high yields in the production of bioproducts. High ethanol yields can be achieved because the entire fraction of hexoses and pentoses are metabolized. In some studies, fermentation can be carried out together with the action of different strains. The fermentation in two processes is also an alternative, first the microorganisms act on the hexoses and then on the pentoses (Yadav et al. 2011; Santosh et al. 2017; Mirfakhar et al. 2020; Mishra and Ghosh 2020). Table 2.1 shows several studies with different plant biomasses, in which ethanol production was carried out with the simultaneous fermentation of hexoses and pentoses and with genetically modified microorganisms or with the action of different microorganism strains.

The literature shows several fungi strains that act simultaneously on these sugars, the most cited are *Fusarium*, *Rhizopus*, *Neurospora*, and *Paecilomuces*. Some bacteria are also reported to carry out the fermentation of pentoses and hexoses, i.e., *Escherichia coli*, *Klebsiella*, *Bacillus*, *Aeromonas*, *Lactobacillus,* and *Clostridium* (Novy et al. 2013; Yadav et al. 2011; Kumar et al. 2018).

**Table 2.1** Co-fermentation and co-culture strategies to improve bioethanol production

| Lignocellulosic material | Hydrolysis conditions | Microbial strains | Ethanol (g/g) | References |
|---|---|---|---|---|
| Co-fermentation of corn stover | Hydrothermal process | *Escherichia coli* FBR 5 | 0.49 | Saha et al. (2015) |
| Co-fermentation of yellow poplar | Oxalic acid treatment | *Pichia stipitis* CBS 6054 | 0.49 | Kundu et al. (2015) |
| Co-fermentation of olive tree pruning | Diluted phosphoric acid | *Escherichia coli* MS04 | 0.46 | Martínez-Patiño et al. (2017) |
| Co-fermentation of sugar cane bagasse | HTP and post-hydrolysis with sulfuric, maleic and oxalic acids | *Scheffersomyces stipitis* NRRL Y-7124 | 0.31 | Nakasu et al. (2016) |
| Co-fermentation of rice straw | Diluted acid ($H_2SO_4$) | *Saccharomyces cerevisiae, SXA-R2P-E* | 0.43 | Ko et al. (2016) |
| Co-fermentation of D-xylose and L-arabinose | Purified form of D-xylose e L-arabinose | Recombinant *Saccharomyces cerevisiae* | 0.43 | Caballero and Ramos (2017) |
| Co-fermentation of sugar cane bagasse | Diluted acid ($H_2SO_4$) | *Escherichia coli LW419a* and *Saccharomyces cerevisiae* | 0.46 | Wang et al. (2019) |
| Co-fermentation of glucose and xylose | No | *Saccharomyces cerevisiae* | 0.36 | Nakamura et al. (2008) |
| Co-fermentation<br>Corn stover | Diluted acid ($H_2SO_4$) | *Saccharomyces cerevisiae* | 0.41 | Zhu et al. (2016) |
| Co-fermentation of wheat straw | Modified *Saccharomycs cerevisiae* TMB3400, KE6-12 and KE6-13i | *Saccharomyces cerevisiae* | 0.46 | Erdei et al. (2013) |
| Co-culture fermentation of kans grass | Diluted acid ($H_2SO_4$) | *Zymomonas mobilis* and *Scheffersomyces shehatae* | 0.43 | Mishra and Ghosh (2020) |
| Co-fermentation of rice straw | Diluted acid ($H_2SO_4$)<br>Microwave assisted alkali | *Pichia stipitis* 3498 | 0.47 | Sheetal et al. (2019) |
| Co-fermentation of sugar cane bagasse | Acid and steam | *Kluyveromyces marxianus IIPE453* | 0.31 | Dasgupta et al. (2017) |
| Co-fermentation of *Agave lechuguilla* | Diluted acid ($H_2SO_4$) | *Escherichia coli MM160* | 0.37 | Díaz-Blanco et al. (2018) |
| Co-fermentation of rapeseed straw | Diluted acid ($H_2SO_4$) | Industrial *Saccharomyces cerevisiae NAPX37* | 0.38 | Li et al. (2017) |

(continued)

**Table 2.1** (continued)

| Lignocellulosic material | Hydrolysis conditions | Microbial strains | Ethanol (g/g) | References |
|---|---|---|---|---|
| Co-culture fermentation of glucose and xylose | No | *Zymomonas mobilis* and *Scheffersomyces stipitis* | 0.48 | Nguyen et al. (2019) |
| Co-culture fermentation of rice straw | Sodium hydroxide and autoclave | *Saccharomyces cerevisiae* and *Scheffersomyces stipitis* | 0.47 | Suriyachai et al. 2013 |
| Co-culture fermentation of wheat straw | Hydrothermic process | *Fusarium oxysporum* and *Saccharomyces cerevisiae* | 0.41 | Paschos et al. (2015) |
| Co-culture fermentation of pomegranate peel | Diluted acid ($H_2SO_4$) | *Saccharomyces cerevisiae* and *Pichia stipitis* | 0.43 | Demiray et al. (2018) |

The yeasts *Pichia stipitis*, *Candida shehatae,* and *Pachysolen tannophilus* are also used to co-ferment pentoses and hexoses, however, in tests with ethanol concentrations higher than 30–35 g $L^{-1}$ the metabolism of *P. stipitis* is inhibited, which may be a problem when applied in large-scale processes (Gutiérrez-Rivera et al. 2012; Robak and Balcerek 2020). Besides, wild strains or genetically modified yeasts metabolize first glucose and then xylose when they are exposed to media with a mixture of sugars. In many cases only with the transformation of glucose, there is already an ethanol content at the limit tolerated by these yeasts. This fact avoids the full metabolization of the fraction of xyloses, influencing ethanol yield, making it difficult to improve the process (De Bari et al. 2013; Wirawan et al. 2020). Thus, processes with the joint action of more than one microorganism can be employed, aiming to increase ethanol yields, bringing viability to the process and providing the use of the total fraction of pentoses and hexoses, through co-cultures.

The immobilization of microorganisms has been a strategy used to improve co-culture processes, using immobilization in porous matrices and surface adsorption, cross-linking, and hydrogel encapsulation. The main strains used are immobilized *Z. mobilis* and free *P. stipitis. Z. mobilis* uses the glucose fraction and *P. stipitis* uses the xylose fractions, enabling an increase in the yield of bioethanol production (Liu and Dong 2020; Wirawan et al. 2020).

The use of specific enzymes for action on lignocellulosic biomass is also reported. These microbial hemicellulases are obtained by fungi such as *Aspergillus*, producing xylanases, which are recognized for their high potential to modify and transform these lignocellulosic biomasses. The main action of xylanases is the degradation of cellulose fractions and the use of these enzymes as a pretreatment reduces the use of chemicals. Furthermore, they can replace the use of chemical pretreatments, decreasing the generation of toxic by-products after the degradation of the biomass structures (Michelin et al. 2013; Abdella et al. 2020).

It is noticed that most of the studies were carried out using chemical pretreatments (Table 2.1), using strategies to improve the process in the fermentation phase, as these chemical pretreatments are already known for being efficient in releasing the compounds of these lignocellulosic raw materials. However, they have disadvantages, mainly in their adverse conditions of execution, demanding high amounts of energy and reagents. The challenge is to seek the optimization of these enzymatic or ionic pretreatments with co-culture and co-fermentation strategies (D'Amato et al. 2017; Hassan et al. 2019; Garlapati et al. 2020).

The increasing development of research aiming to evaluate the entire ethanol production cycle from lignocellulosic biomass has been bringing new technologies and the emergence of optimized processes with high yields such as those listed in Table 2.1. Advances in biotechnology and metabolic engineering bring the concepts of biorefinery and circular bioeconomy, strengthening the entire ethanol production cycle, giving greater viability, profitability, and fewer generations of waste or by-products. Thus, processes such as co-fermentation and co-culture of microorganisms can improve the generation of ethanol using the fermentation of hexoses and pentoses. Besides, new pretreatment methodologies and production of specific enzymes can be used, aiming at better yields, which would provide a closure of the production cycle, bringing the advances of biorefinery and circular bioeconomy to the production of bioethanol from these raw materials.

## 2.4 Conclusion and Final Remarks

As shown in this chapter, the concepts of sustainability, circular bioeconomy, and biorefineries are of great interest in the development of products that benefit society in our present and future from biomass. The processing of this biomass through hydrothermal processes is a great alternative at a pilot and industrial level that will continue to be used for the fractionation of biomass. On the other hand, the hemicellulosic fraction represents an important raw material in the production of high added value compounds, which today are of great relevance in the bioeconomy in different areas such as food (films and coatings, xylooligosacharides, xylitol) bioenergy (bioethanol) and fine chemicals (furfural). Techno-economic studies and life cycle analysis (LCA) of biomass fractionation processes and products are necessary to find sustainable alternatives.

**Acknowledgements** Financial support from the Energy Sustainability Fund 2014-05 (CONACYT-SENER), Mexican Centre for Innovation in Bioenergy (Cemie-Bio), Cluster of Bioalcohols (Ref. 249564) is gratefully acknowledged. We also gratefully acknowledge support for this research by the Mexican Science and Technology Council (CONACYT, Mexico) for the infrastructure project—INFR201601 (Ref. 269461) and CB-2015-01 (Ref. 254808).

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# Production of Hemicellulosic Sugars from Residual Lignocellulosic Biomass in an Integrated Small-Scale Biorefinery: Techno-Economic and Life Cycle Assessments

# 3

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## Abstract

Biorefineries design, as for other industries, usually target the economy of scale approach, maximizing processing capacities to achieve economic viability. However, the installation of large-scale biorefineries has some drawbacks, namely their high capital costs and the difficulty to assure a proper supply of biomass at regional level. Small-scale, self-sustainable, biorefineries can solve several of the challenges of their larger competitors and are also reported to expand environmental and social benefits, but several hurdles for their deployment still exist.

This chapter describes a methodology for the implementation of an integrated small-scale self-sustainable biorefinery in a rural area, based on a design that takes advantage of the synergies of processing two types of feedstock (corn stover and swine manure). A detailed explanation for the process selection by performing a heuristic analysis, process simulation, mass and energy balances alongside with the techno-economic assessment of the biorefinery is provided. The full life cycle assessment (LCA) of producing xylo-oligosaccharides (XOS) and ethanol from lignocellulosic residues, i.e. corn stover, under a biorefinery concept to be located in Portugal is also assessed.

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M. Brienzo (ed.), *Hemicellulose Biorefinery: A Sustainable Solution for Value Addition to Bio-Based Products and Bioenergy*, Clean Energy Production Technologies, https://doi.org/10.1007/978-981-16-3682-0_3

**Keywords**

Lignocellulosic residues · Hemicellulosic sugars · Biorefinery · Life cycle assessment · Xylo-oligosaccharides · Ethanol

## 3.1 Introduction

Biorefineries have initially followed the concept of traditional, crude oil based, refineries, targeting the use of only a single feedstock within plants presenting large processing capacities in order to achieve economic sustainability through an economy of scale approach. Under this framework, most rural areas in Europe and even worldwide fail to sustain effective conditions to install such biorefineries. Several studies point out that high CAPEX and OPEX are the main bottlenecks, together with the inability of most regions to support per se a sustainable large supply of biomass (Chandel et al. 2018). An alternative approach relies on the onset of small-scale biorefineries in rural areas. These would be able to overcome most of these challenges, strengthening territorial economic cohesion and generating local direct and indirect jobs (de Visser and van Ree 2016). Small-scale enables a substantial cost reduction related to feedstock transportation, as well as of intermediate products leading to a direct link between the primary sector and industry, supporting the bioeconomy onset and progress. In spite of the recognized strategic importance of small-scale biorefineries, there are still various technological, operational, and policy challenges hampering their commercial deployment (Balan 2014). For instance, in temperate and tropical regions, there is a great diversity of bio-resources (ranging from crop and forestry residues to animal waste, and industrial agro-food processing residues) that lack proper logistic and political support, as well as technological solutions to enable their concomitant valorization.

A possible technological strategy to tackle this diversity/heterogeneity is the combination of two or more of the diverse biorefinery platforms: the use of (a) typical biochemical platform processes to transform lignocellulosic feedstock into sugars and lignin-rich streams that can be concomitantly converted into biofuels (e.g. bioethanol or higher alcohols), and/or added-value chemicals, and (b) the anaerobic digestion platform converting wet biomass and side streams into biogas (Bharathiraja et al. 2016). The later can be upgraded into biomethane and sold or used for plant own consumption. This example of a small-scale integrated biorefinery is able to take advantage of both dry and wet bio-resources to produce a significant portfolio of diverse bioproducts, thus maximizing feedstock utilization, energy efficiency, and overall sustainability of the whole value chain.

Under this framework, the lignocellulosic biomass pre-treatment is an important and often restrictive step for the efficient processing of biomass in a biorefinery, being the hydrothermal processes (e.g., autohydrolysis) a clean and efficient pathway for the production of two upgradable streams: the liquid stream, hemicellulose-rich, and on the other hand, the solid cellulose-rich stream (Gírio et al. 2010). Oligosaccharides, particularly xylo-oligosaccharides (XOS), as emerging food additives presenting many functional properties (most noteworthy, the prebiotic effect), can be targeted as the high added-value product from the hemicellulose-rich liquor (Samanta et al. 2015; Moniz et al. 2016; Gullón et al. 2017; Turck et al. 2018). Bioethanol can be targeted as the main bulk products to be derived from the cellulose-rich solid fraction.

This chapter proposes and assesses the advantages of such small-scale, integrated biorefinery. It follows a heuristic analysis for best scenario selection, and the subsequent detailed process modelling and simulation using computer-aided process engineering tools to ascertain process feasibility at industrial scale (Moncada et al. 2013; Mussatto et al. 2013; Quintero et al. 2013). The influence of external factors in the economic sustainability of such a small-scale biorefinery, the identification of the major factors impacting its environmental sustainability, and the legal framework for its implementation are also assessed.

## 3.2 Heuristic Analysis

When assessing the economic and environmental viability of a biorefinery, it is important to evaluate the possible scenarios on a preliminary basis. Thus, a heuristic approach related with the design of a biorefinery system using the available feedstock, preliminary mass balances, process scale, matureness level of technologies, and product competitors must be performed beforehand (Cardona Alzate et al. 2004, 2019).

The following procedure is recommended to be applied in case studies with the purpose of justifying and better understanding the small-scale biorefineries potential, before proceeding to detailed Process Modelling and Simulation.

### 3.2.1 Feedstock

(a) Availability—The feedstock's availability (type of residues, available amount per year, etc.) for each selected region shall be evaluated.

(b) Accessibility—The accessibility to the selected feedstock in terms of logistics, annual production, competing uses, shall be assessed.

### 3.2.2 Biorefinery Design

Based on the chosen feedstock and expertise in biomass/bioproducts transformation, a preliminary knowledge-based conceptual design was applied. For this, a preliminary process flowsheet for the biorefinery case-study was built, as it is shown in the example of Fig. 3.1.

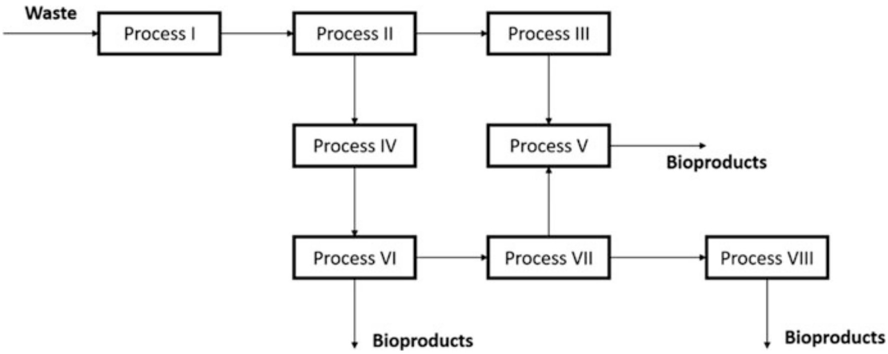

**Fig. 3.1** Example of a typical biorefinery flowsheet

### 3.2.3 Preliminary Assessments

After building a first scenario for the biorefinery design, a preliminary mass and energy balance with the available feedstock for each region shall be performed.

These preliminary balances will help to select the process scale, based on the total amount of final product that can be produced using the available feedstock and the biorefinery design scenario.

Furthermore, a preliminary economic assessment shall be performed to predict scenarios viability under the selected conditions. For that, the most representative operating costs (OPEX) must be calculated as well as the main equipment capital costs (CAPEX). The economic viability can be assessed by calculating the net present value (NPV[1]) for a selected scale, being economically viable when NPV $> 0$.

### 3.2.4 Process Scale Selection

Afterwards, the biorefinery scale (that shall be small-scale[2]) should defined using one of the following options (Serna-Loaiza et al. 2019):

A. Define a range (minimum and maximum) based on the availability and accessibility of feedstock.

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[1] NPV—Net Present Value: NPV $= \sum_{n=0}^{n=\text{project lifetime}} \frac{\text{Cash Flow}}{(1+\text{interest})^n}$ (Sadhukhan et al. 2014)

[2] Small-scale was defined by comparison of the amount of final product obtained with the produced amount in industrial scale of the same products, that for the present analysis should differ at least in one order of magnitude. For the cases where more than one product is obtained, the same approach is applied to the biomass processed.

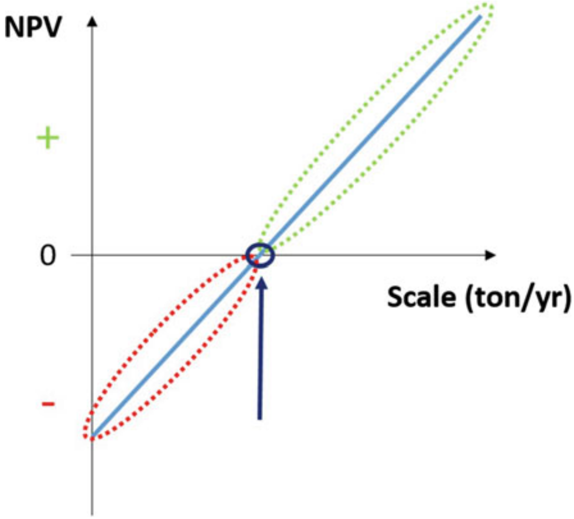

**Fig. 3.2** Example of net present value variation with process scale

B. Find the minimum process scale to have NPV (net present value) > 0 and evaluate what can be improved in the process for scales where NPV < 0 (Fig. 3.2).
C. Fix the scale (at a small-scale basis).

All this analysis can be performed without any in-depth calculations and just using literature, previous experience, and basic preliminary calculations.

### 3.2.5 Process Technologies Choice

After selecting the scale, the biorefinery design must be improved, and the unit operations choice properly justified. For the Biorefinery Process Design in a case study, the choice of the unit operations should be based on these aspects: (a) final product quality (market requirement) and (b) technology matureness at industrial scale.

The matureness of technologies on industrial plants (small-scale) can be categorized in three different levels:

- Level 1—Type of technology with relatively low exploitation in the industry; R&D work.
- Level 2—Technology already exploited in the industry but not fully optimized.
- Level 3—Mature technology at industrial scale, fully established.

For each possible scenario, the matureness level of each technology shall be listed to help with a final decision on the most appropriate pathway to follow. As an example, Table 3.1 presents an assessment of a hypothetical scenario within an

**Table 3.1** Example of the matureness level assessment of the technologies

| Unit operation | Pressing | Reverse osmosis | Ultra-filtration | Electrodialysis | Ion exchanger | ... |
|---|---|---|---|---|---|---|
| Matureness level | 3 | 2 | 2 | 1 | 2 | ... |

assessment. The chosen technologies for the whole process should be listed and categorized on their matureness at industrial scale.

Technologies with matureness level "1" must be *totally avoided* when designing a small-scale biorefinery. Only for specific cases, when no other options are available or, for instance, if it is the only known type of technology to obtain the required product purity, etc. Technologies with matureness level "2" should only be used if properly justified (based on energy consumption, product properties, process restrictions, subsequent units' requirements, etc.). Technologies with matureness level "3" have no restrictions.

### 3.2.6 Evaluation of Product Competitors

Product selection and biorefinery design shall be evaluated also based on the final product competitors in the region under assessment:

(a) One shall assess the market needs and specificities for the possible products for the feedstock in the region or in the surrounding regions, and evaluate the existing competitors.
(b) Different scenarios should be assessed based on different possible products, added-value products, energy/heat production, etc. The scenario choice must be justified based on the revenues, the competitors' sale price, the logistics (product transport and distribution to the buyers).

Figure 3.3 shows an example of different scenarios based on the possible products that can be obtained and a comparison based on the achieved profit.

### 3.2.7 Process Modelling

Once all steps described from 2.1 to 2.6 are complete, and the process design is properly justified and established, it will be able to proceed to detailed Process Modelling and Simulation using a commercial software like Aspen Plus (Aspen Technology, Inc.), SuperPro Designer (Intelligen, Inc.), or similar.

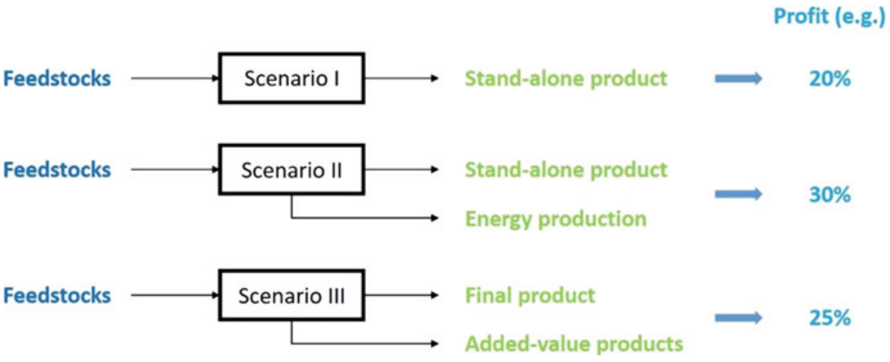

**Fig. 3.3** Example of different scenarios based on different biorefinery products

**Table 3.2** Feedstock characterization

| Component | Value | Units |
|---|---|---|
| Glucan | 40.83 | % |
| Xylan | 23.48 | % |
| Arabinan | 3.06 | % |
| Lignin | 16.91 | % |
| Others | 15.72 | % |

### 3.2.8 Application of the Heuristic Approach to the Case-Study

This case-study consists in an integrated small-scale biorefinery to be developed in Portugal. This assessment has considered the available residual lignocellulosic biomass and high-carbon content biomass for anaerobic digestion in the continental territory, and the possible synergies within the rural areas.

#### 3.2.8.1 Available Feedstock

Portugal has very advantageous conditions for corn cultivation, presenting productivities that can exceed 14 ton/ha (*ANPROMIS* 2020), ranking among the highest worldwide. The main agricultural residues from this crop are the cobs and stalks, including leaves, typically called corn stover, which can account between 70 and 90%, by weight, of the produced corn grain, depending on the agricultural productivity, with higher grain productivities presenting a lower residue to grain ratio. Currently, these residues are mainly left in the field, taking not only a long time to be degraded, but also having significant impact on greenhouse gas production. In Portugal, about 110,000 ha of the best available soils are used for corn cultivation (Instituto Nacional de Estatística, 2018). Therefore, corn residues (namely corn stover) have great potential for being used in a biorefinery concept.

For the base-case scenario and in a 50 km radius around Chamusca region (ca. 25 km north from Lisbon, Portugal), ca. 100,000 ton/year of dry corn stover (Table 3.2) are available (200,000 ton/year if 100 km radius is considered). Regarding the accessibility to the feedstock (logistics, annual production, competitors, etc.), around 30% of the total amount at least is considered to be accessible to be used within the biorefinery. Therefore, 30,000 ton/year of corn stover is the minimum available dry biomass feedstock. Furthermore, in this region there are also many livestock farms producing important amounts of swine manure.

### 3.2.8.2 Biorefinery Design

The dominating strategy for fuel ethanol production from biomass (Gírio et al. 2010) relies on the initial removal of hemicellulose from the lignocellulosic materials. This fraction is extremely relevant to the economic feasibility of a lignocellulosic biomass-based biorefinery, not only by the co-fermentation of hemicellulose together with cellulose sugars can lead to higher amounts of bioethanol, but mainly through the production of oligosaccharides and/or monomeric sugars.

Thus, having that into account and based on the chosen feedstock, the following four scenarios were assessed:

- **Scenario A** (Fig. 3.4): solid and liquid fractions are separated. Liquid fraction (hemicellulose) is concentrated by evaporation in order to produce **pentose molasses**. Solid fraction (cellulose-rich, cellulolignin) is subject to enzymatic hydrolysis and fermented to produce **ethanol** via separate hydrolysis and fermentation (SHF) or simultaneous saccharification and fermentation (SSF);

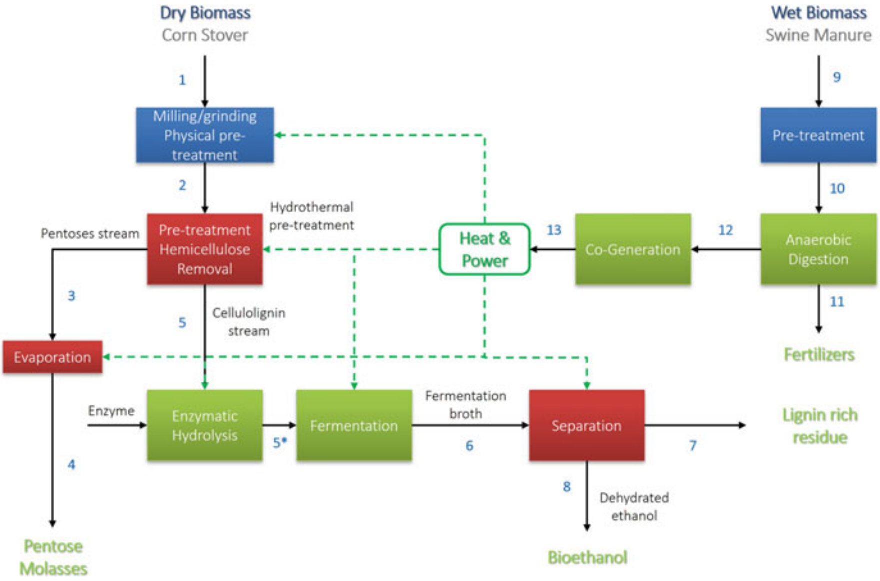

**Fig. 3.4** Simplified block flow diagram of the processes involved in Scenario A

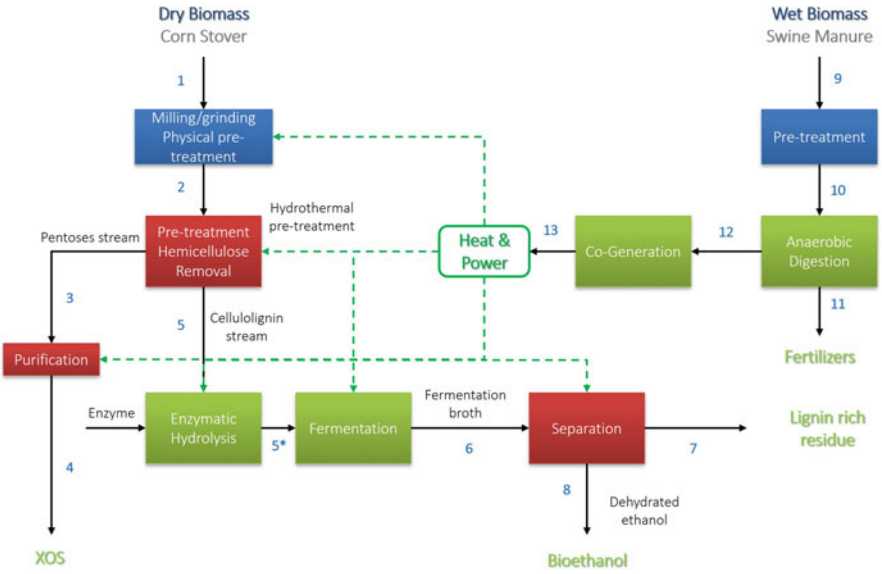

**Fig. 3.5** Simplified block flow diagram of the processes involved in Scenario A′

- **Scenario A′** (Fig. 3.5): liquid fraction (hemicellulose) undergoes a purification step using membranes, in order to obtain **xylo-oligosaccharides** (XOS), besides producing **ethanol** from solid fraction (cellulolignin);
- **Scenario B** (Fig. 3.6): the slurry obtained after pre-treatment follows a pre-liquefaction with enzymes and is then fermented in a SSCF mode (simultaneous saccharification and co-fermentation of pentoses and hexoses) to produce **ethanol**;
- **Scenario C** (Fig. 3.7): liquid fraction (hemicellulose) is conveyed to acid post-hydrolysis step in order to obtain monomeric sugars (mainly pentoses) that will be converted to **xylitol** by a yeast strain. The solid fraction is processed as in scenario A to produce **ethanol**.

As mentioned before, associated to these agriculture crops, there are also livestock farms producing important amounts of swine manure that must be treated for environmental reasons and which can also be used for energetic valorisation using anaerobic digestion.

The process consists in the degradation of the organic matter, contained in the piggery effluents, and its conversion into a digested flow and a gaseous flow energy carrier (**biogas**). Through this process, the effluents are valorised and the negative environmental impacts associated to pig farming practice are avoided. The products of the anaerobic digestion—digested stream for irrigation and soil fertilization and

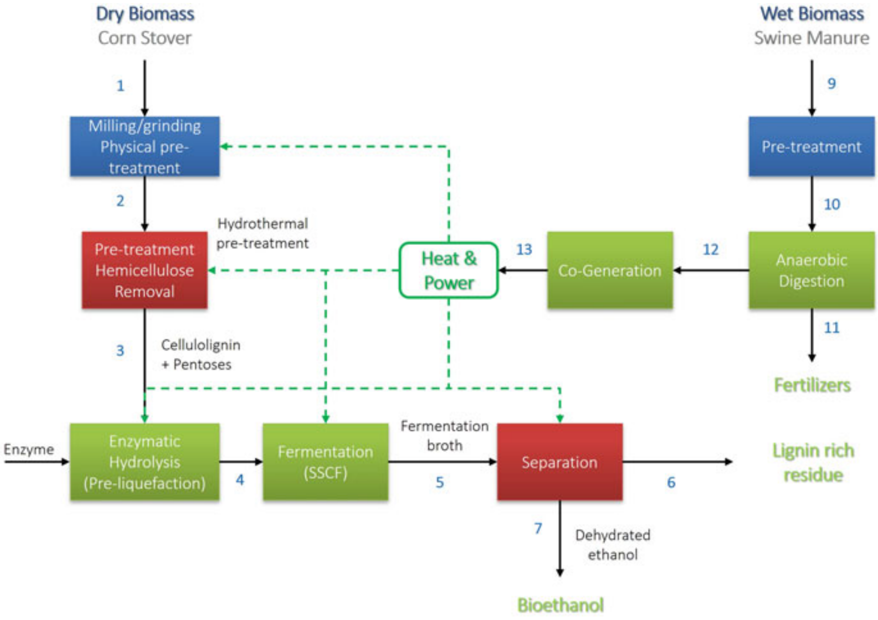

**Fig. 3.6** Simplified block flow diagram of the processes involved in Scenario B

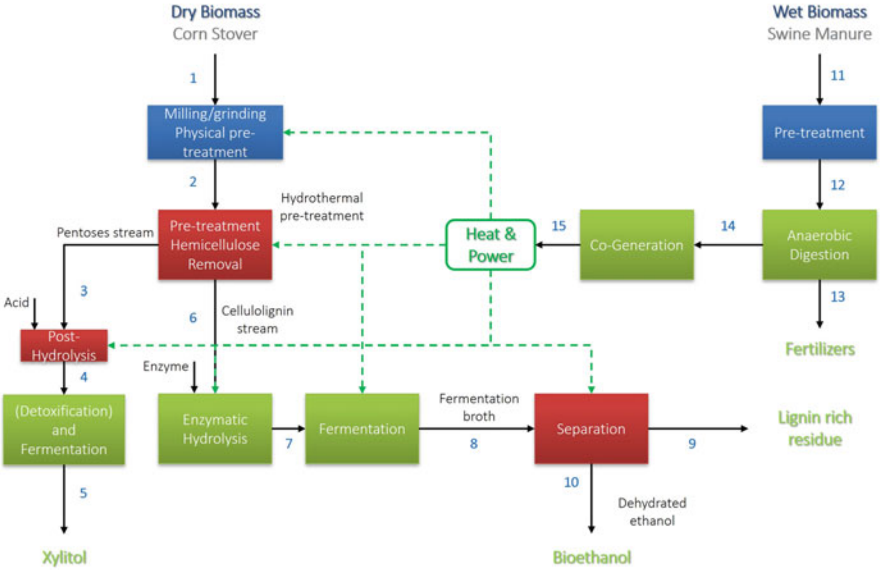

**Fig. 3.7** Simplified block flow diagram of the processes involved in Scenario C

energy carrier gas, useful to **heat/power/fuel gas**—are applied to contribute in the best way to the sustainability of the whole process.

#### 3.2.8.3 Technology Matureness Level

Regarding the industrial matureness level of the assessed scenarios, the leading technologies were evaluated. For Scenario A (Table 3.3) all technologies are well established at an industrial level. In Scenario A′ (Table 3.4), XOS purification is still under pilot-scale development; thus, the level 2 was attributed for the separation step. In Scenario B (Table 3.5), the co-fermentation of C5/C6 sugars is not yet completely established at an industrial scale, so that a level 2 was also attributed to SSCF. Finally, for Scenario C (Table 3.6) also, the fermentation step was also classified with level 2 as only few industrial plants are using this procedure.

#### 3.2.8.4 Preliminary Assessments

After the selection of scenarios, the identification of possible products, and the evaluation of the matureness of the technologies involved, preliminary mass and energy balances must be performed, as previously described, for proper comparison between scenarios.

**Table 3.3** Matureness level at industrial scale for the used technologies in Scenario A

| | Technologies/unit operations | | | |
|---|---|---|---|---|
| Scenario A | Milling | Hemicellulose removal | SHF/SSF | Separation |
| Matureness level | 3 | 3 | 3 | 3 |

**Table 3.4** Matureness level at industrial scale for the used technologies in Scenario A′

| | Technologies/unit operations | | | | |
|---|---|---|---|---|---|
| Scenario A′ | Milling | Hemicellulose removal | SHF/SSF | Separation | Purification |
| Matureness level | 3 | 3 | 3 | 3 | 2 |

**Table 3.5** Matureness level at industrial scale for the used technologies in Scenario B

| | Technologies/unit operations | | | | |
|---|---|---|---|---|---|
| Scenario B | Milling | Hemicellulose removal | Purification | SSCF | Separation |
| Matureness level | 3 | 3 | 3 | 2 | 3 |

*SSCF* simultaneous saccharification and co-fermentation

**Table 3.6** Matureness level at industrial scale for the used technologies in Scenario C

| | Technologies/unit operations | | | | | |
|---|---|---|---|---|---|---|
| Scenario C | Milling | Hemicellulose removal | Post-hydrolysis | Detoxification | SHF | Separation |
| Matureness level | 3 | 3 | 3 | 3 | 2 | 3 |

**Table 3.7** Experimental data used for heuristic analysis

| Item | Units | Scenario | | | |
|---|---|---|---|---|---|
| | | A | A′ | B | C |
| Glucan recovery | % | 90 | 90 | 90 | 90 |
| Hemicellulose recovery | % | 30 | 30 | 30 | 30 |
| Cellulose pre-liquefaction | % | 80 | 80 | 80 | 80 |
| Hemicellulose pre-liquefaction | % | 70 | 70 | 70 | 70 |
| Ethanol yield (SHF) | g/g Glc | 0.51 | 0.51 | – | 0.51 |
| Ethanol yield from glucose (SSCF) | g/g Glc | – | – | 0.51 | – |
| Ethanol yield from xylose (SSCF) | g/g Xyl | – | – | 0.41 | – |
| Fermentation efficiency | % | 90 | 90 | 90 | 90 |
| Glucose assimilation | % | 100 | 100 | 100 | 100 |
| Lignin recovery (AH[a]) | % | 85 | 85 | 85 | 85 |
| Lignin recovery (SHF) | % | 90 | 90 | 90 | 90 |
| Lignin sep. efficiency | % | 100 | 100 | 100 | 100 |
| XOS yield | % | 60 | 60 | 60 | – |
| XOS recovery | % | – | 60 | 60 | – |
| Post-hydrolysis yield | % | – | – | – | 95 |
| Xylose assimilation | % | – | – | – | 95 |
| Xylitol yield | % | – | – | – | 51 |
| Xylitol recovery | % | – | – | – | 90 |
| Steam for heating | ton/ton | 1.0 | 1.0 | – | – |
| Steam for pre-treatment | ton/ton | 0.25 | 0.25 | 0.25 | 0.25 |
| Steam for post-hydrolysis | ton/ton | – | – | – | 0.1 |
| Ethanol purity | % | 99.5 | 99.5 | 99.5 | 99.5 |

[a] *AH* autohydrolysis

Although this is a preliminary assessment, some experimental data must be applied to achieve more accurate conclusions. Table 3.7 presents the relevant experimental data required to determine the mass and energy balances in each scenario.

Taking into account the simplified flowsheets presented before, the mass balances were calculated and are presented in Tables 3.8, 3.9, 3.10, and 3.11, for scenarios A, A′, B, and C.

For the energy balances, the heating required for pre-treatment in all scenarios and for post-hydrolysis (scenario C) was considered, considering the data shown in Table 3.7.

Subsequently, a preliminary economic assessment shall be performed. Since the calculation of detailed capital investment costs is very time consuming, a simplification can be achieved by correlating reported CAPEX in literature for several biorefinery plants, with different capacities (Table 3.12 and Fig. 3.8). A polynomial correlation between these two variables can be adjusted and is represented by the Eq. (3.1) ($R^2 = 0.93$).

**Table 3.8** Preliminary mass balance for Scenario A

| Compounds (dry basis) | Streams (ton/year) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3&4 | 5 | 5* | 6 | 7 | 8 |
| Corn stover | 30,000 | 30,000 | – | – | - | – | – | – |
| Glucan | – | 12,249 | – | 11,024 | 2205 | 2205 | 2205 | – |
| Xylan | – | 7044 | – | 2113 | 634 | 634 | 634 | – |
| Arabinan | – | 918 | – | 275 | 83 | 83 | 83 | – |
| Lignin | – | 5073 | – | 4312 | 4312 | 3881 | 3881 | – |
| Others | – | 4716 | – | – | – | – | – | – |
| XOS | – | – | 4777 | – | 1672 | 1672 | – | 1672 |
| GlcOS | – | – | 1225 | – | – | – | – | – |
| Molasses | – | – | 6002 | – | – | – | – | – |
| Lignin-rich solid | – | – | – | – | 7233 | 6802 | 6802 | – |
| Glucose | – | – | – | – | 9799 | – | – | – |
| Ethanol | – | – | – | – | – | 4498 | – | 4475 |

**Table 3.9** Preliminary mass balance for Scenario A′

| Compounds (dry basis) | Streams (ton/year) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 5* | 6 | 7 | 8 |
| Corn stover | 30,000 | 30,000 | – | – | – | – | – | – | – |
| Glucan | – | 12,249 | – | – | 11,024 | 2205 | 2205 | 2205 | – |
| Xylan | – | 7044 | – | – | 2113 | 634 | 634 | 634 | – |
| Arabinan | – | 918 | – | – | 275 | 83 | 83 | 83 | – |
| Lignin | – | 5073 | – | – | 4312 | 4312 | 3881 | 3881 | – |
| Others | – | 4716 | – | – | – | – | – | – | – |
| XOS | – | – | 4777 | 2866 | – | 1672 | 1672 | – | 1672 |
| GlcOS | – | – | 1225 | – | – | – | – | – | – |
| Molasses | – | – | 6002 | – | – | – | – | – | – |
| Lignin-rich solid | – | – | – | – | – | 7233 | 6802 | 6802 | – |
| Glucose | – | – | – | – | – | 9799 | – | – | – |
| Ethanol | – | – | – | – | – | – | 4498 | – | 4475 |

$$\text{Correlation for CAPEX vs.Plant Capacity : CAPEX} = 0.5571 \times \text{Plant Capacity (ton/year)}^{0.4912} \tag{3.1}$$

Regarding OPEX, these will depend on the operating units considered for each scenario. Feedstock costs, operating costs of process units, and labour were the components considered for the OPEX calculation. Table 3.13 summarizes the OPEX estimates for processing 30,000 ton/year of corn stover for each scenario. In Table 3.13 are also presented the CAPEX costs for each scenario using the same annual amount of feedstock, which results in equal costs regardless the scenario

**Table 3.10** Preliminary mass balance for Scenario B

| Compounds (dry basis) | Streams (ton/year) 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| Corn stover | 30,000 | 30,000 | – | – | – | – | – |
| Glucan | – | 12,249 | 11,024 | 2205 | 2205 | 2205 | – |
| Xylan | – | 7044 | 2113 | 634 | 634 | 634 | – |
| Arabinan | – | 918 | 275 | 83 | 83 | 83 | – |
| Lignin | – | 5073 | 4312 | 3881 | 3881 | 3881 | – |
| Others | – | 4716 | – | – | – | – | – |
| XOS | – | – | 4777 | 1433 | 1433 | – | 1433 |
| GlcOS | – | – | 1225 | 245 | 245 | – | 245 |
| Lignin-rich solid | – | – | 17,725 | 6802 | 6802 | 6802 | – |
| Glucose | – | – | – | 10,888 | – | – | – |
| Xylose | – | – | – | 5016 | 1003 | 1003 | – |
| Ethanol | – | – | – | – | 6471 | – | 6439 |

since the previously presented correlation was used, in which the CAPEX only depends on the scale.

Regarding preliminary economic assessment, Scenario B, in which hemicellulose and cellulose streams that are obtained from biomass pre-treatment are processed together, leads to lower OPEX due to the absence of hemicellulose fraction independent valorisation. On the other hand, Scenario A and A′ have higher OPEX due to the hemicellulose fraction separation, being the latter higher due to the xylo-oligosaccharides valorisation. Scenario C, due to the post-hydrolysis step presents the highest OPEX among the assessed scenarios.

#### 3.2.8.5 Process Scale and Scenario Selection

After concluding the preliminary assessments, the most promising scenario and the most adequate scale must be selected based on process economic feasibility, along with the previously referred items. The economic feasibility, as described above, is assessed by determining the NPV versus process scale. For the NPV calculation, the revenues as well as some economic factors (e.g., interest rate, plant lifetime) shall be taken into account. The data used for the preliminary assessment is summarized in Table 3.14. These data are based on feedstock costs including transport. Products' market prices and financial parameters were also conservatively estimated, based on diverse data sources (see below).

Figure 3.9 shows the NPV variation with the process scale (within the available feedstock amount) for the assessed scenarios. One can observe that Scenario A and Scenario B are not economically viable (NPV $< 0$) for any scale, while Scenario A′ is viable for any scale and Scenario C for scales higher than 40,000 ton/year of corn stover.

After concluding all the steps of the heuristic analysis, one can conclude that Scenario A′ and Scenario C are the most promising pathways for the corn stover-based biorefinery. Nonetheless, due to high added value of xylo-oligosaccharides

**Table 3.11** Preliminary mass balance for Scenario C

| Compounds (dry basis) | Streams (ton/year) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| Corn stover | 30,000 | 30,000 | – | – | – | – | – | – | – | – |
| Glucan | – | 12,249 | – | – | – | 11,024 | 2205 | 2205 | 2205 | – |
| Xylan | – | 7044 | – | – | – | 2113 | 634 | 634 | 634 | – |
| Arabinan | – | 918 | – | – | – | 275 | 275 | 275 | 275 | – |
| Lignin | – | 5073 | – | – | – | 4312 | 3881 | 3881 | 3881 | – |
| Others | – | 4716 | – | – | – | – | – | – | – | – |
| XOS | – | – | 4226 | – | – | – | – | – | – | – |
| GlcOS | – | – | 1225 | – | – | – | – | – | – | – |
| Lignin-rich solid | – | – | – | – | – | – | 6995 | 6995 | 6995 | – |
| Xylose | – | – | – | 4563 | 228 | – | 1900 | 1900 | – | 1900 |
| Xylitol | – | – | – | – | 1990 | – | – | – | – | – |
| Glucose | – | – | – | 1293 | – | – | 9799 | – | – | – |
| Ethanol | – | – | – | – | – | – | – | 4498 | – | 4475 |

**Table 3.12** Capital investment and ethanol volume production of biorefinery plants reported in literature

|  | Technology used |  | Production |  |  |  |
|---|---|---|---|---|---|---|
| Plant | Pre-treatment | Fermentation | Feedstock (Mton/ year) | Ethanol (mil L/ year) | CAPEX (M. USD) | References |
| Clariant | Uncatalyzed Steam Explosion | SSCF | 4.5 | 1.3 | 34.2 | Clariant (2017) |
| CIMV | Organosolv | SSCF | 9.0 | 1.1 | 68.3 | Delmas (2015) |
| BioGasol | Steam Explosion | SSCF | 27.0 | 7.0 | 61.0 | *BioGasol* (2017) |
| Inbicon | Autohydrolysis | SSF/SSCF | 30.0 | 5.4 | 78.1 | Persson (2013) |
| Biochemtex (Crescentino) | Uncatalyzed Steam Explosion | n/a | 270.0 | 50.0 | 183.0 | *Betarenewables* (2017) |
| POET-DSM | Acid-catalyzed Steam Explosion | SSCF | 285.0 | 75.0 | 298.9 | *POET-DSM* (2017) |
| Maabjerb Energy Center | n/a | n/a | 300.0 | 80.0 | 292.8 | *MEC* (2017) |
| Abengoa (Hugoton Plant) | Acid-catalyzed Steam Explosion | SSCF | 350.0 | 94.0 | 378.2 | ABENGOA (2013) |
| GRANBIO | Uncatalyzed Steam Explosion | SSCF | 400.0 | 82 0.0 | 323.3 | GranBio (2017) |

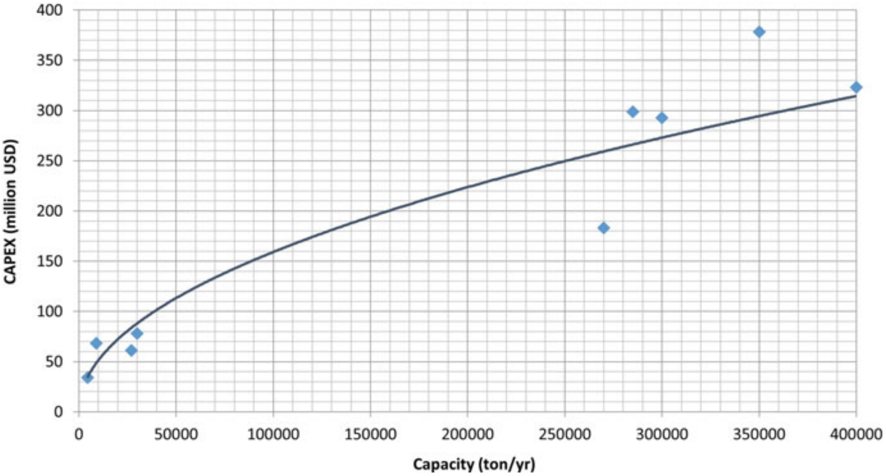

**Fig. 3.8** Variation of capital investment costs with plant capacity, according to literature data

and its emerging market as prebiotics (Samanta et al. 2015), Scenario A′ is the most adequate route to assess in detail.

Following, the selected scenario shall be modelled using software-based tools for process engineering, for detailed mass and energy balances and equipment mapping, and consequently, a complete techno-economic analysis. Subsequently, an environmental assessment shall follow to validate the biorefinery sustainability.

## 3.3 Detailed Process Design and Simulation

The integrated corn stover (LCB)[3] and swine manure (ADB)[4] based biorefinery was simulated using Aspen Plus v10.0 (Aspen Technology, Inc., USA) to establish the requirements for feedstock, utilities, and energy. Physico-chemical properties of cellulose, hemicellulose, lignin, enzyme, and yeast were based on the NREL database (Wooley and Putsche 1996). The Non-Random Two Liquids (NRTL) thermodynamic model was used for the simulation of the behaviour of the liquid phases. The Hayden O'Connell equation of state was selected to represent the vapour phase (Quintero et al. 2013). The simulation was run based on product concentrations and yields from LNEG experimental data and from literature.

The flowsheet of the corn stover/swine manure integrated biorefinery is shown in Fig. 3.10, and it is divided into nine distinct sections: (1) Drying and milling; (2) Pre-treatment; (3) Enzymatic hydrolysis; (4) Fermentation; (5) Bioethanol

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[3] LCB—lignocellulosic biorefinery.

[4] ADB—anaerobic digestion biorefinery.

**Table 3.13** Example of preliminary OPEX estimates for the assessed scenarios for a scale of 30,000 ton/year

| Scenario A | ton/year | Price (USD/ton) | Annual total (M.USD/year) |
|---|---|---|---|
| *1. Feedstock* | | | |
| Corn stover | 30,000.0 | 54.9 | 1.65 |
| Enzymes | | 185.5[a] | 0.83 |
| *2. Operating costs* | | | |
| Distillation | 4475.3 | 79.3 | 0.35 |
| Pre-treatment (heating) | 37,500.0 | 12.2 | 0.46 |
| Drying/evaporation | 146,768.1 | 12.2 | 1.79 |
| *3. Labour* | | | |
| Personnel costs | | | 0.85 |
| **Total OPEX** (Scenario A) (Million USD/year) | | | **5.93** |
| **Total CAPEX** (Scenario A) (Million USD) | | | **88.12** |
| Scenario A′ | ton/year | Price (USD/ton) | Annual total (M.USD/year) |
| *1. Feedstock* | | | |
| Corn stover | 30,000.0 | 54.9 | 1.65 |
| Enzymes | | 185.5 | 0.83 |
| *2. Operating costs* | | | |
| Distillation | 4475.3 | 79.3 | 0.35 |
| Pre-treatment (heating) | 37,500.0 | 12.2 | 0.46 |
| Purification (XOS) | 156,002.1 | 9.8 | 1.52 |
| Drying/evaporation | 78,001.1 | 12.2 | 0.95 |
| 3. Labour | | | |
| Personnel costs | | | 0.85 |
| **Total OPEX** (Scenario A′) (Million USD/year) | | | **6.62** |
| **Total CAPEX** (Scenario A′) (Million USD) | | | **88.12** |
| Scenario B | ton/year | Price (USD/ton) | Annual total (M.USD/year) |
| *1. Feedstock* | | | |
| Corn Stover | 30,000.0 | 54.9 | 1.65 |
| Enzymes | | 185.5 | 1.19 |
| *2. Operating costs* | | | |
| Distillation | 6438.8 | 79.3 | 0.51 |
| Pre-treatment (heating) | 37,500.0 | 12.2 | 0.46 |
| *3. Labour* | | | |
| Personnel costs | | | 0.85 |
| **Total OPEX** (Scenario B) (Million USD/year) | | | **4.66** |
| **Total CAPEX** (Scenario B) (Million USD) | | | **88.12** |
| Scenario C | ton/year | Price (USD/ton) | Annual total (M.USD/year) |
| *1. Feedstock* | | | |
| Corn Stover | 30,000.0 | 54.9 | 1.65 |
| Enzymes | | 185.5 | 0.83 |
| *2. Operating costs* | | | |
| Distillation | 4475.3 | 79.3 | 0.35 |
| Pre-treatment (heating) | 37,500.0 | 12.2 | 0.46 |

(continued)

**Table 3.13** (continued)

| Scenario C | ton/year | Price (USD/ton) | Annual total (M.USD/year) |
|---|---|---|---|
| Acid hydrolysis ($H_2SO_4$) | 1500.0 | 104.9 | 0.16 |
| Post-hydrolysis treatment | 12,000.0 | 12.2 | 0.15 |
| Neutralization ($Ca(OH)_2$) | 2268.4 | 85.4 | 0.19 |
| Xylitol prod. and purif. | 1989.5 | 1509.1 | 3.00 |
| *3. Labour* | | | |
| Personnel costs | | | 1.28 |
| **Total OPEX** (Scenario C) (Million USD/year) | | | **8.07** |
| **Total CAPEX** (Scenario C) (Million USD) | | | **88.12** |

[a]Per ton of ethanol produced

**Table 3.14** Market prices, feedstock availability, and economic factors considered for the preliminary economic feasibility assessment

| Market prices[a] | USD/ton | Feedstock (corn stover) | ton/year |
|---|---|---|---|
| Feedstock | 54.90 | Minimum | 30,000 |
| Ethanol | 732.00 | Maximum | 100,000 |
| Lignin | 54.90 | **Economic factors** | |
| Pentose molasses | 164.70 | Payback period (years) | 5 |
| XOS | 4270.00 | Interest rate | 0.05 |
| Xylitol | 4392.00 | Plant lifetime (years) | 20 |

[a]Estimates

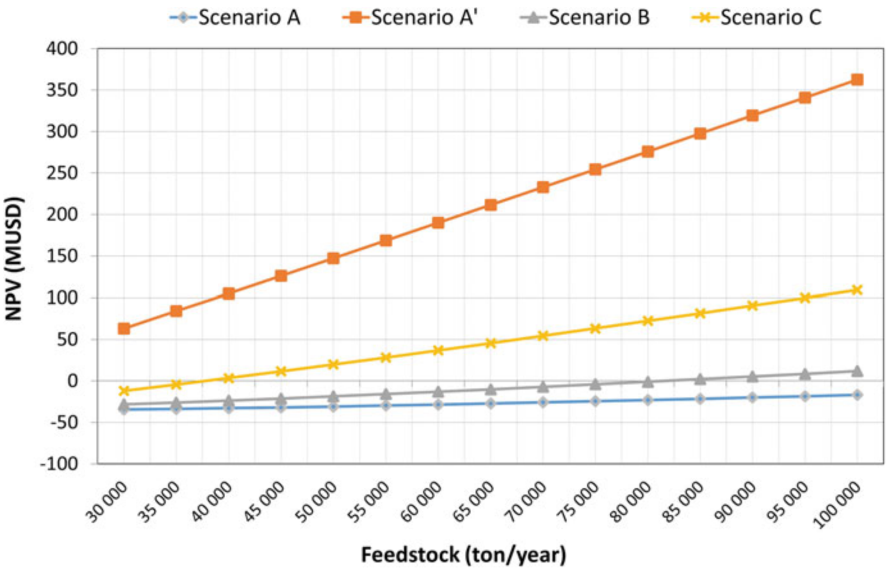

**Fig. 3.9** Net present value versus the amount of processed feedstock for each scenario assessed

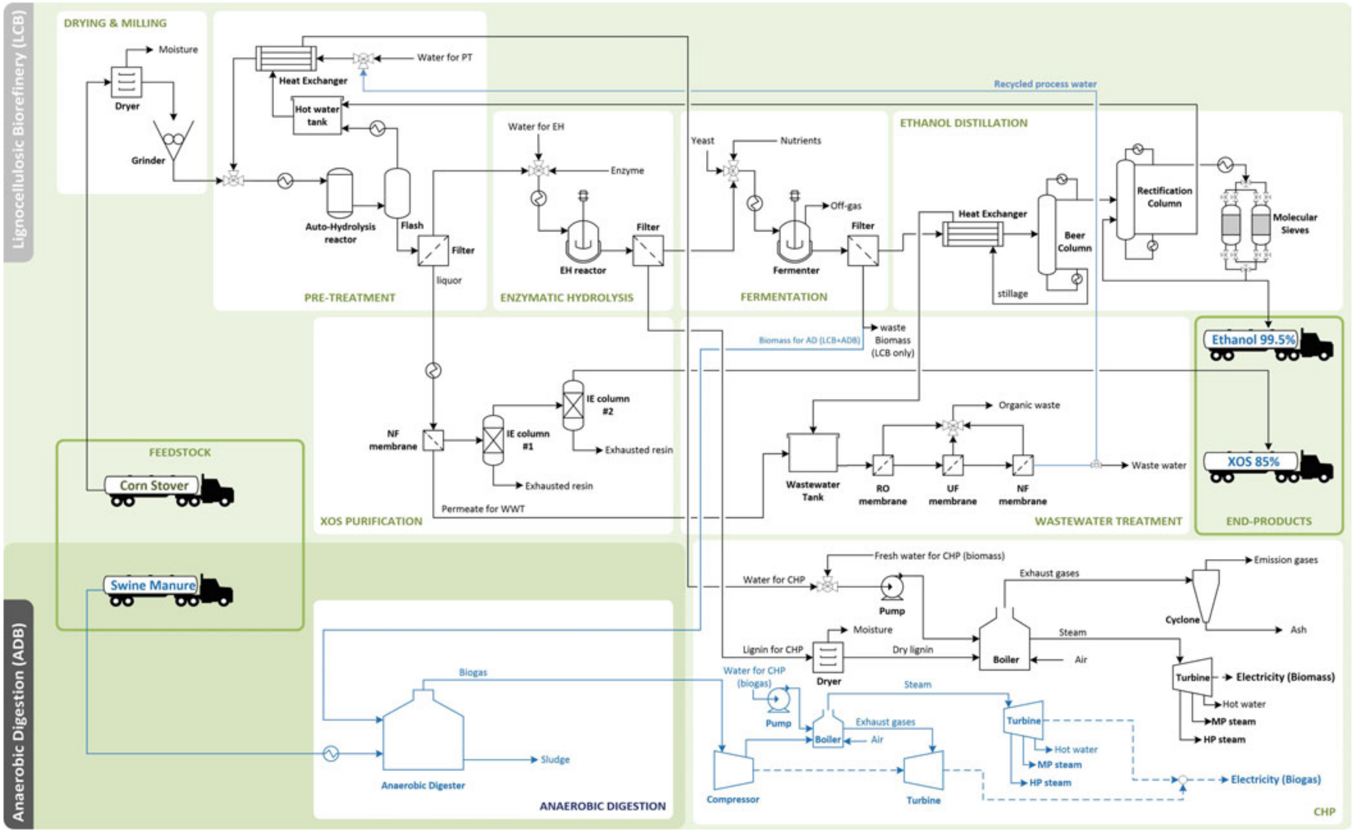

**Fig. 3.10** Flowsheet scheme of the LCB and ADB for the selected scenario

**Table 3.15** Autohydrolysis reactions and conversions

| Reaction | Fractional conversion of component | Fractional conversion | References |
|---|---|---|---|
| Cellulose + $H_2O$ → Glucose | Cellulose | 0.024 | Moniz (2014) |
| Cellulose → GlcOS | Cellulose | 0.035 | Moniz (2014) |
| Cellulose → HMF + $2H_2O$ | Cellulose | 0.002 | Moniz (2014) |
| Xylan + $H_2O$ → Xylose | Xylan | 0.030 | Moniz et al. (2013) |
| Xylan → XOS | Xylan | 0.560 | Moniz et al. (2013) |
| Xylan → Furfural +$2H_2O$ | Xylan | 0.016 | Moniz et al. (2013) |
| Arabinan + $H_2O$ → Arabinose | Arabinan | 0.317 | Moniz et al. (2013) |
| Arabinan → AOS | Arabinan | 0.285 | Moniz et al. (2013) |
| Acetate → Acetic Acid | Acetate | 0.307 | Moniz et al. (2013) |
| Lignin → Soluble Lignin | Lignin | 0.150 | Moniz et al. (2013) |

*GlcOS* gluco-oligosaccharides, *XOS* xylo-oligosaccharides, *AOS* arabino-oligosaccharides

distillation and dehydration; (6) Xylo-oligosaccharides purification; (7) Wastewater treatment; (8) Anaerobic digestion, and (9) Combined Heat and Power generation.

## 3.3.1 Process Modelling

As available feedstock, 100,000 ton/year of corn stover was considered [dry weight basis: 40.2% of cellulose, 28.5% of hemicellulose, 20.8% of lignin, 2.9% protein and 1.5% of extractives] and 125 $m^3$/day of swine manure with 5% solids was also taken into account for the simulation procedure. Operation conditions and yields used as process parameters are described in the following sections.

### 3.3.1.1 Drying and Milling

First, corn stover is air-dried from an initial moisture of 20% to a final moisture of 10%. The lignocellulosic biomass is then milled (to particles below 6 mm) using a crusher.

### 3.3.1.2 Pre-treatment

Milled corn stover is conveyed to a hydrothermal pre-treatment (autohydrolysis) step for hemicellulose removal. The autohydrolysis is carried out using high-pressure steam (autogenous pressure of 19 bar at 210 °C) in a steam to solid ratio of 8:1. The considered hydrolysis reactions and conversions are presented in Table 3.15.

Upon completion of the autohydrolysis process, the solid and liquid fractions are separated. The liquid fraction (liquor) is subjected to a purification step for xylo-oligosaccharides recovery. The solid fraction is conveyed to the enzymatic hydrolysis step.

#### 3.3.1.3 Enzymatic Hydrolysis

A separate hydrolysis and fermentation system was chosen. As previously referred, the solid fraction is recovered after pre-treatment and undergoes an enzymatic hydrolysis (EH) process. EH is run at 50 °C using Cellic CTec2® (Novozymes) at an enzyme loading of 20 mg $g^{-1}$ of cellulose, and a total solid loading of 20% for 72 h (NREL 2011). The considered EH reactions and conversions are presented in Table 3.16.

#### 3.3.1.4 Fermentation

Afterwards, the temperature is cooled to 32 °C in order to enable the fermentation step, where 1 $g_{DW}$ $L^{-1}$ (10 vol% of production vessel size) of *Saccharomyces cerevisiae* is used to inoculate the mixture. After 24 h from inoculation, a yield of 0.48 $g_{ethanol}$ ${g_{glucose}}^{-1}$ is obtained (Gírio and Fonseca 2015). The considered reactions for this step are presented in Table 3.17.

#### 3.3.1.5 Ethanol Distillation and Dehydration

At the end of the fermentation, the broth is conveyed to the ethanol recovery section. This contains two distillation columns and one molecular sieve. The first column, called the beer column, takes ethanol concentration up to 60 wt% in the distillate, while the stillage (column bottoms) is conveyed to the wastewater treatment section after pre-heating the beer column feed. The second column, called rectification column, ethanol is to bring up to the azeotrope (93 wt%), while the column bottoms are sent to a hot water collector to pre-heat the water before the pre-treatment, and then sent to CHP for steam generation. In order to go beyond the azeotrope, the ethanol stream is sent to a molecular sieve until reaching a concentration of 99.5 wt% (fuel grade).

#### 3.3.1.6 Xylo-Oligosaccharides Purification

The oligomers-rich liquor from pre-treatment undergoes a purification step with membranes. Firstly, the stream is cooled down to 90 °C and then goes through a

**Table 3.16** Chemical reactions and fractional conversions considered for the enzymatic hydrolysis step

| Reaction | Fractional conversion of component | Fractional conversion | References |
|---|---|---|---|
| Cellulose + $H_2O$ → Glucose | Cellulose | 0.80 | Gírio and Fonseca (2015) |
| Xylan + $H_2O$ → Xylose | Xylan | 0.70 | Gírio and Fonseca (2015) |

**Table 3.17** Chemical reactions and fractional conversions considered for the ethanologenic fermentation step

| Reaction | Fractional conversion of component | Fractional conversion | References |
|---|---|---|---|
| Glucose → 2Ethanol + $2CO_2$ | Glucose | 0.950 | NREL (2011) |
| Glucose + $2H_2O$ → 2Glycerol + $O_2$ | Glucose | 0.004 | NREL (2011) |
| Glucose + $2CO_2$ → 2Succinic Acid + $O_2$ | Glucose | 0.006 | NREL (2011) |
| Glucose + $0.0208SO_4^{2-}$ + $1.3705NH_4^+$ → 5.9603*S. cerevisiae* + $3.7945H_2O$ | Glucose | 0.020 | NREL (2011) |

nanofiltration membrane, followed by two subsequent ionic exchanging steps to reach xylo-oligosaccharides with 85% purity (Vegas et al. 2006, 2008).

#### 3.3.1.7 Wastewater Treatment

The relevant wastewater streams, namely the permeate from the xylo-oligosaccharides purification, and the stillage from ethanol distillation, are mixed together. This mixed stream presents a low chemical oxygen demand (COD), and hence neither anaerobic nor aerobic digestion are suitable for its treatment. Thus, this stream is processed through membrane technology-based system comprising reverse osmosis, ultra-filtration, and nanofiltration to separate sugars, organics, and microorganisms from water. This allows a 90% recovery of the water back into the process. The remaining 10% are purged from the system.

#### 3.3.1.8 Anaerobic Digestion

Spent yeast and swine manure undergoes a pre-heating process to reach 32 °C before being fed into the anaerobic digester, which is run at atmospheric pressure with a residence time of 30 days. The biogas ($CH_4$ and $CO_2$) yields assumed in the simulation process are presented in Table 3.18.

#### 3.3.1.9 Combined Heat and Power Generation

The residual lignin obtained after the filtration of liquefaction (enzymatic hydrolysis) broth is sent to the power and heat generation section (CHP). After being dried until 5% moisture, it is fed into a boiler (1540 °C) for the production of high-pressure steam (HP, 24 bar), medium-pressure stream (MP, 7 bar), and hot water, as well as electricity. Table 3.19 presents the combustion reactions for lignin as well as for the

**Table 3.18** Conversions considered for the anaerobic digestion reactor

| Component | Yield (mass fraction) | Reference |
|---|---|---|
| $CH_4$ | 0.56 | LNEG experimental data |
| $CO_2$ | 0.24 | LNEG experimental data |
| Non-converted sludge | 0.10 | LNEG experimental data |

**Table 3.19** Chemical reactions and fractional conversions considered for the CHP section

| Reaction | Fractional conversion of component | Fractional conversion | Ref. |
|---|---|---|---|
| Lignin + $10.125O_2 \rightarrow 7.3CO_2 + 6.95H_2O$ | Lignin | 1 | Wooley and Putsche (1996) |
| Cellulose + $6O_2 \rightarrow 6CO_2 + 5H_2O$ | Cellulose | 1 | Wooley and Putsche (1996) |
| Xylan + $5O_2 \rightarrow 5CO_2 + 4H_2O$ | Xylan | 1 | Wooley and Putsche (1996) |

residual hemicellulose and cellulose. The biogas from the Anaerobic Digestion is compressed up to 16 bar before being burned in a second boiler (2170 °C) to also generate HP, MP, hot water, and electricity.

### 3.3.2 LCB Only

For comparison reasons, a LCB-only scenario was also modelled. Under this scenario, the generated lignin is not enough to fulfil the process energy (electricity) needs by burning it in CHP, thus there is no electricity surplus. A detailed flowsheet for this scenario is represented in Fig. 3.11.

### 3.3.3 Results

Table 3.20 summarizes the mass balances obtained from the Aspen Plus model for the selected scenario, while Table 3.21 presents the energy balances. One can observe that by processing 100 kton/year of lignocellulosic residues (corn stover), ca. 12 kton/year of bioethanol together with ca. 8.3 kton/year of high purity xylo-oligosaccharides are produced. Regarding the utility needs in energy balances, a high amount of high-pressure steam is required for the pre-treatment and cooling water for the ethanol recovery. However, the integration with ADB leads to an electricity generation surplus that can be sold, for higher revenues, to the grid.

## 3.4 Techno-Economic Assessment

### 3.4.1 Methodology

The capital (CAPEX) and operating costs (OPEX) estimates were obtained using the Aspen Economic Analyzer tool (v8.4). For the calculations, a project lifetime of 20 years was considered based on the reports for most industrial chemical processes (Peters et al. 2003; *Trading Economics* 2017), and the straight-line depreciation method was applied. All economic parameters used in this assessment are related to Portuguese context, such as cost of raw materials, income tax, labour, product price, etc. More specifically, it was considered an income tax value of 21% (corporate tax in Portugal), and an annual interest rate of 2% (current rate for Portugal is around 0, thus a more conservative value was taken into account). Table 3.22 presents the economic data for raw material, products, and utilities.

The economic viability of the selected biorefinery was evaluated taking into account the Net Present Value (NPV). Following the *six-tenths-factor rule*, Eq. (3.2) (Peters et al. 2003), the influence of the process scale (amount of Corn Stover to be processed, up to 100 kton/year—maximum available amount in Chamusca region) was also assessed. This analysis can help to decide which range of processing capacity is the most adequate for positive profitability margins.

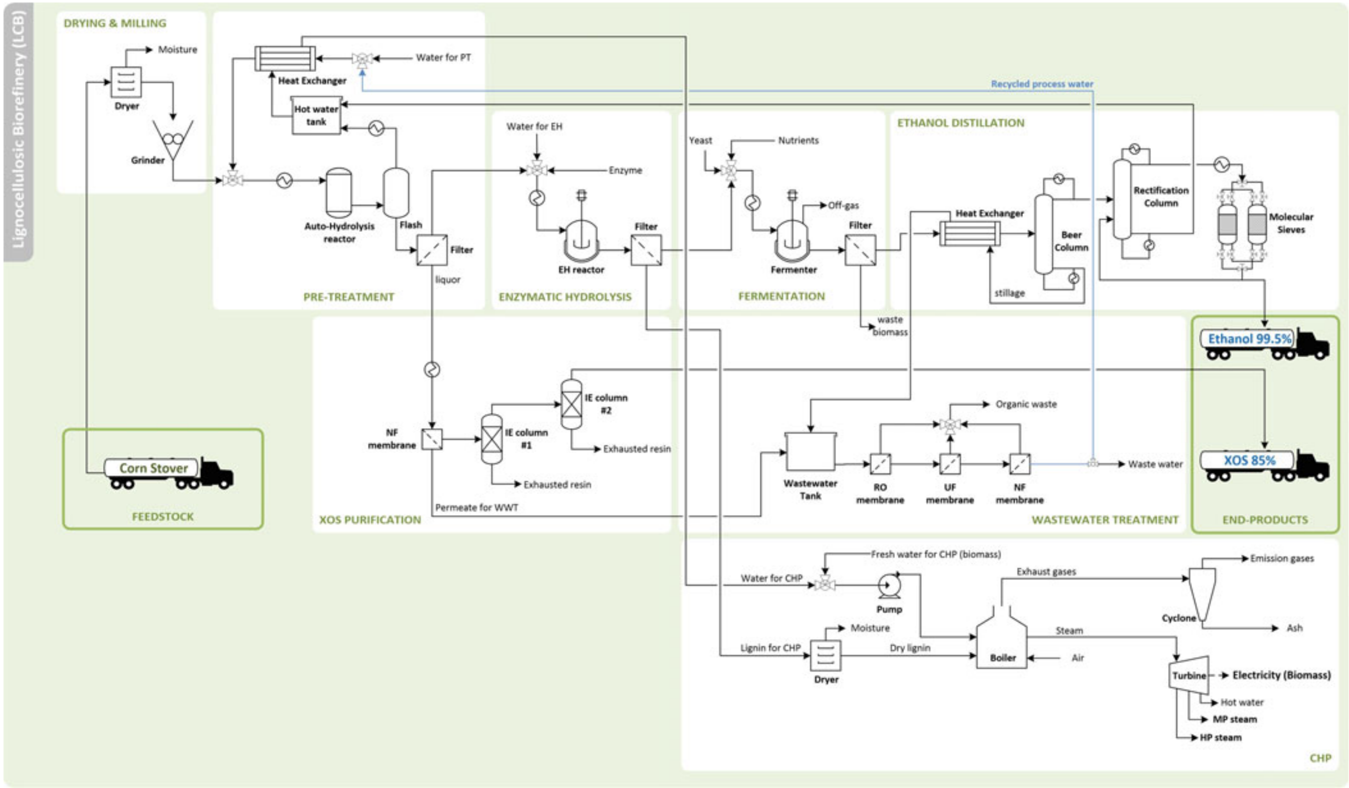

**Fig. 3.11** Flowsheet scheme of the LCB (only) for the selected scenario

**Table 3.20** Mass balances for the assessed biorefinery scenario obtained from process simulation

| Inputs | ton/year | Outputs | ton/year |
|---|---|---|---|
| Corn stover | 100,000 | Ethanol (99.5%) | 12,008 |
| Swine manure | 46,482 | XOS (85%) | 8345 |
| Water (pre-treatment) | 56,939 | Moisture | 18,758 |
| Water (EH) | 138,491 | *Off-gas* ferm. | 11,807 |
| Nutrients | 1376 | Gas emissions | 1,567,470 |
| Yeast | 25,857 | Ash | 2901 |
| Enzyme | 614 | Organic waste | 18,819 |
| Air CHP (biogas) | 716,848 | Digestate | 11,763 |
| Air CHP (biomass) | 769,728 | Ion exchange waste | 2866 |
| Water (CHP) | 600,980 | Water purge | 50,050 |

**Table 3.21** Energy balances for the assessed biorefinery scenario obtained from process simulation

| Utilities | ton/year |
|---|---|
| HP steam | 64,300 |
| MP steam | n/a |
| LP steam | 10,364 |
| Cooling water | 2,633,785 |
| Electricity (process) (MW) | 30 |
| Prod. CHP (biogas) (MW) | 22 |
| Prod. CHP (biomass) (MW) | 28 |
| Electricity process (surplus) (MW) | 20 |

$$\text{Six-tenths-factor rule} : \text{Cost Equip.A} = \text{Cost Equip.B} \times \left(\frac{\text{Capacity A}}{\text{Capacity B}}\right)^{0.6} \tag{3.2}$$

### 3.4.2 Results

Figure 3.12 represents the impact of the plant capacity in the biorefinery profitability (NPV). It can be observed an increase of the NPV along with plant capacity, as expected. However, the amount of corn stover processed shall be higher than 40,000 ton/year for the plant to be economically viable. A payback period of ca. 2 years is expected when processing 100,000 ton/year of corn stover, being higher (ca. 9 years) for the lowest profitable scale (40,000 ton/year) which is almost half the lifetime considered for the project (20 years). The profitability is very sensitive to several variables, most noteworthy, products' market price, and the costs of the raw materials. Figure 3.13 presents the effect of a variation in these costs in the NPV of the project for the scenario of 100,000 ton/year of corn stover processed. One can conclude that the market price of XOS has the highest impact in process viability, since a reduction of ca. 35% of the considered selling price for XOS will make the process as economically non-viable (NPV $< 0$).

**Table 3.22** Market prices of the raw material, utilities, and products

| Compound | Value | Unit |
|---|---|---|
| Corn stover | 52.10[a] | USD/ton |
| Swine manure | 20.26[b] | USD/ton |
| Yeast | n.d.[c] | n.d. |
| Enzyme | 176.10[d] | USD/ton |
| Ethanol | 694.71 | USD/ton |
| XOS | 4052.48[e] | USD/ton |
| Xylitol | 4168.26[e] | USD/ton |
| Electricity | 0.051[f] | USD/MJ |
| Process water | 0.36[g] | USD/$m^3$ |
| Cooling water | 0.13[h] | USD/$m^3$ |
| High-pressure steam | 9.86[i] | USD/ton |
| Mid-pressure steam | 8.18[i] | USD/ton |
| Low-pressure steam | 7.56[i] | USD/ton |

[a] Price includes an estimate for transportation costs of corn stover from crops

[b] Price includes an estimate for transportation (between Chamusca and Lisbon, ca. 25 km)

[c] Not considered for the economic assessment

[d] Data for Novozymes Cellic® CTec3 (*Quora* 2017)

[e] Estimated based on current market prices for XOS-derivatives

[f] Price of electricity in Portugal (ERSE 2018)

[g] Average price in Portugal (*EPAL* 2017)

[h] Price estimated using correlations from (Ulrich and Vasudevan 2006)

[i] Estimates from Aspen Plus software

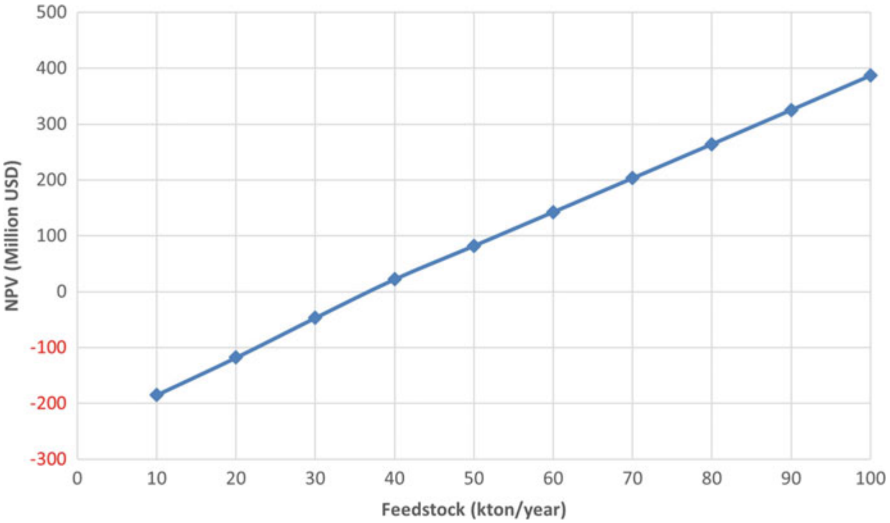

**Fig. 3.12** Influence of the plant capacity in the Net Present Value for the LCB and ADB integrated biorefinery

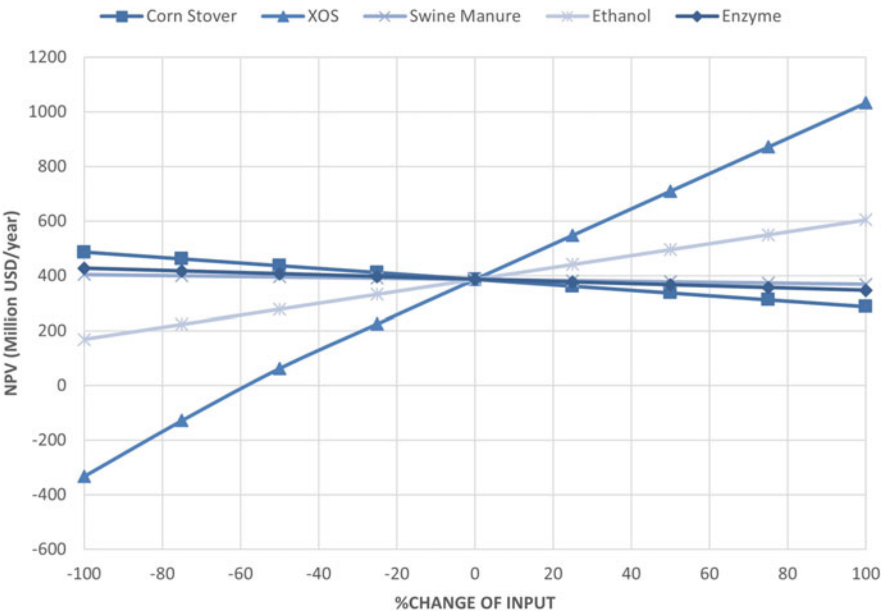

**Fig. 3.13** Influence of the prices of raw materials and products in the NPV for the LCB and ADB integrated biorefinery

**Table 3.23** Comparison between production costs and selling price per product of the integrated biorefinery (100,000 tons of corn stover per year)

| Products | Production costs (USD/ton) | Selling price (USD/ton) | Profit margin (%) |
|---|---|---|---|
| Ethanol | 448.06 | 950.00 | 112.0 |
| XOS | 1911.34 | 4052.48 | |
| Electricity (USD/kWh) | 0.03 | 0.06 | |

From the previous analysis, it is possible to calculate the production costs for the main biorefinery products. Table 3.23 shows the production costs for ethanol, xylo-oligosaccharides, and surplus electricity and the corresponding selling prices. A profit margin of ca. 112% is obtained for each product.

The effect of the ADB platform was assessed by the variation of different amounts of swine manure (within the available range—up to 46,480 ton/year). Figure 3.14 shows the CAPEX and the payback time variation with the amount of feedstock processed.

The process is still economically viable when using LCB only. The use of swine manure results in a higher CAPEX and generates an electricity surplus. By not using the ADB platform (swine manure = 0), a deficit of electricity is observed, and a need for electricity from the grid results in higher OPEX and lower revenues, which leads to higher payback times.

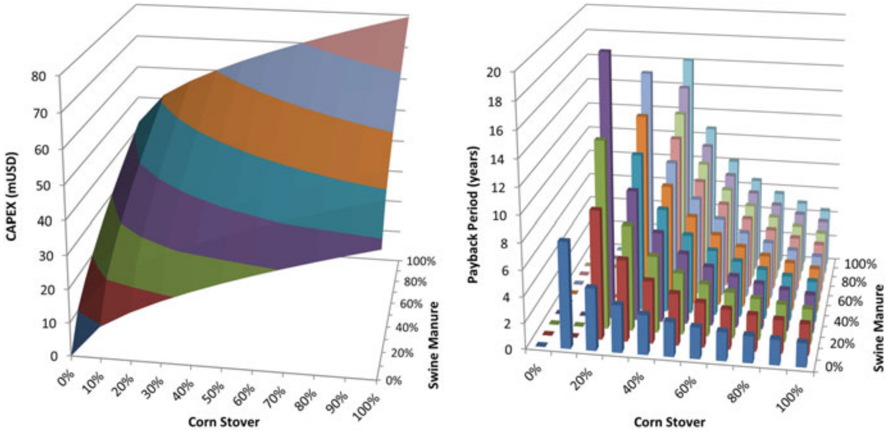

**Fig. 3.14** Variation of the CAPEX (left) and payback period (right) with the amount of feedstock (corn stover and swine manure) used in the biorefinery

## 3.5 Life Cycle Assessment

### 3.5.1 Goal and Scope

For the selected scenario, the environmental impacts related to a biorefinery based in corn stover (CS) as dry biomass and swine manure (SM) as wet biomass were evaluated. For that purpose, a Life Cycle Assessment methodology was performed, following ISO 14040:2006.

The functional unit (FU) chosen for the assessment was 1 ton of lignocellulosic biomass, and the system boundaries are shown in Fig. 3.15, where a cradle-to-gate approach was followed (from corn stover and swine manure recollection to finished products at biorefinery gate). The system was divided in eight sub-systems: corn stover and swine manure recollection and transport (SS0a and SS0b, respectively), biomass pre-treatment (SS1), ethanol production (SS2), ethanol purification (SS3), XOS production (SS4), anaerobic digestion (SS5), wastewater treatment (SS6), and cogeneration (SS7).

### 3.5.2 Life Cycle Inventory

The system inventory data (inputs and outputs) were obtained from the simulation performed in Aspen Plus. The inventory data for background processes was taken from the Ecoinvent 3.5 database. Table 3.24 resumes the inventory data used for the LCA of this corn stover-based biorefinery. The environmental assessment was performed in SimaPro 9.1 also with Ecoinvent 3.5. The following categories were evaluated using ReCiPe Midpoint (H) methodology: GW—global warming

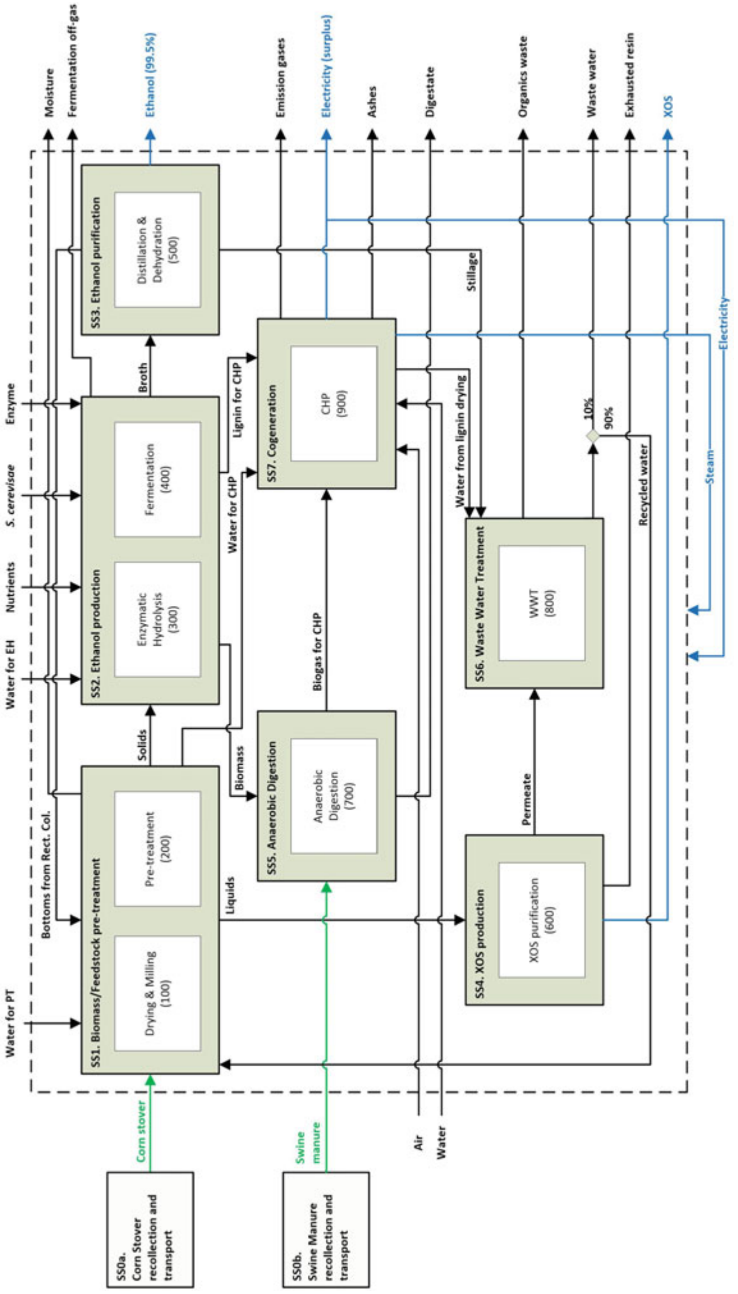

**Fig. 3.15** Simplified flowchart of the corn stover/swine manure biorefinery system

**Table 3.24** Inventory data for the corn stover (CS) and swine manure (SM) integrated biorefinery (values per FU = 1 ton lignocellulosic biomass)

| Inputs | | | Outputs | | |
|---|---|---|---|---|---|
| From the technosphere | | | Products | | |
| CS (SS0) | 1000 | kg | Ethanol (99.5%) | 122.46 | kg |
| CS transport (SS0) | 50.00 | tkm | XOS (85%) | 85.2 | kg |
| SM transport (SS0) | 21.85 | tkm | Electricity | 1.75 | MWh |
| Water to SS1 | 339.06 | kg | *Emissions to the air* | | |
| Water to SS2 | 1384.99 | kg | $H_2O$ (SS1) | 113.34 | kg |
| Ammonium sulphate (SS2) | 10.95 | kg | $CO_2$ (SS2) | 117.66 | kg |
| Water in nutrients (SS2) | 2.76 | kg | $O_2$ (SS2) | 0.45 | kg |
| Yeast (SS2) | 78.16 | kg | $H_2O$ (SS7) | 1578.39 | kg |
| Water in inoculum (SS2) | 182.38 | kg | $CO_2$ (SS7) | 1297.98 | kg |
| Enzyme (SS2) | 6.14 | kg | $O_2$ (SS7) | 565.70 | kg |
| SM (SS5) | 464.85 | kg | CO (SS7) | 5.27 | kg |
| Water for CHP (SS7) | 1451.70 | kg | $N_2$ (SS7) | 9258.24 | kg |
| *From the environment* | | | $H_2$ (SS7) | 0.01 | kg |
| Air for CHP (SS7) | 12,099.49 | kg | $NO_2$ (SS7) | 0.26 | kg |
| | | | NO (SS7) | 51.04 | kg |
| | | | *Wastes to treatment* | | |
| | | | Ion exchanger sludge (SS4) | 32.89 | kg |
| | | | Digester sludge (SS5) | 94.32 | kg |
| | | | Chemical waste (SS6) | 217.33 | kg |
| | | | Ash to landfill (SS7) | 29.01 | kg |

potential, SOD—stratospheric ozone depletion, FPMF—fine particulate matter formation, TA—terrestrial acidification; FE—freshwater eutrophication, ME—marine eutrophication, LU—land use, FRS—fossil resource scarcity, and, finally, WC—water consumption.

### 3.5.3 Environmental Characterization

The corn stover-based biorefinery aims to produce ethanol, xylo-oligosaccharides (XOS), and electricity. Due to this diversity of products, it is necessary to follow an allocation approach to distribute the environmental impacts associated to each product. Due to the different nature of the products (fuel, sugar, and energy), an economic allocation approach was followed. Table 3.25 presents the calculation of the allocation factors in this study, also including the results for mass allocation if electricity production is not taken into account.

In Table 3.26 are summarized the environmental impacts associated to each product, according to the economic allocation described above. Due to the market

**Table 3.25** Calculation of the allocation factors

| Product | Annual production (ton/year) | Market price | | Revenues (M €/year) | Allocation (%) | |
|---|---|---|---|---|---|---|
| | | | | | Mass | Economic |
| Ethanol | 12,009 | 820 | €/ton | 9.84 | 59.0 | 20.2 |
| XOS | 8345 | 3496 | €/ton | 29.18 | 41.0 | 59.9 |
| Electricity (GWh/year) | 175 | 0.08 | €/kWh | 9.66 | – | 19.9 |
| Total | 20,354 | – | | 48.68 | 100 | 100 |

**Table 3.26** Environmental impacts (values per FU = 1 ton lignocellulosic biomass)

| Impact category | Total system | Ethanol | XOS | Electricity |
|---|---|---|---|---|
| GW (kg $CO_2$ eq) | 412.75 | 83.38 | 247.24 | 82.14 |
| SOD (kg CFC11 eq) | $3.14 \times 10^{-5}$ | $6.34 \times 10^{-6}$ | $1.88 \times 10^{-5}$ | $6.24 \times 10^{-6}$ |
| FPMF (kg PM10 eq) | 12.13 | 2.45 | 7.27 | 2.41 |
| TA (kg $SO_2$ eq) | 31.12 | 6.29 | 18.64 | 6.19 |
| FE (kg P eq) | 0.30 | 0.06 | 0.18 | 0.06 |
| ME (kg N eq) | 3.23 | 0.65 | 1.94 | 0.64 |
| LU ($m^2$a crop eq) | 209.55 | 42.33 | 125.52 | 41.70 |
| FRS (kg oil eq) | 80.61 | 16.28 | 48.28 | 16.04 |
| WC ($m^3$) | 8.83 | 1.78 | 5.29 | 1.76 |

price of XOS, the highest contribution for each impact category is attributed to xylo-oligosaccharides.

Figure 3.16 presents the contribution of each subsystem to the environmental impacts. Regarding GW, the highest contributor is SS2 due to the use of yeast. Also, the enzyme and other processes included in SS2 have effect in this impact category. In other categories, such as TA, FE, ME and FPMF, is sub-system SS7 (cogeneration) that has the highest contribution, and this is mainly related to the combustion gases emissions.

### 3.5.4 Effect of the Use of Swine Manure (Wet Biomass)

As described above, in order to evaluate the effect of swine manure in the environmental sustainability of the integrated biorefinery, an alternative system was assessed by not considering the use of swine manure and consequently anaerobic digestion and biogas production. Figure 3.17 represents the process system where SS5 (Anaerobic Digestion) was removed.

Figure 3.18 shows a comparison between both systems (with and without swine manure). It was concluded that the use of swine manure as wet biomass has a positive effect in the biorefinery sustainability. This is due to the fact that when

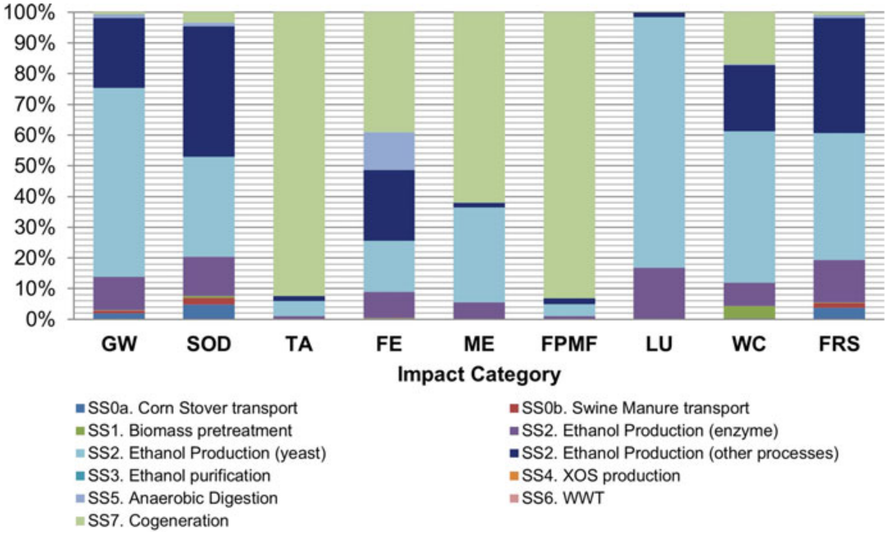

**Fig. 3.16** Sub-systems contribution to the environmental impacts of the corn stover and swine manure based biorefinery

using swine manure, the production of biogas leads to an electricity surplus that can be sold to the grid. However, without swine manure there is the need of buying electricity from the grid and this has a negative effect in almost every impact category.

## 3.6 Legal Framework and Implementation Potential for Rural Areas

Technical, economic, and environmental viability of a new technological route could be inconsequential if there is no legal application for the developed project. In terms of biomass use, the Portuguese Government approved in 2017 four Decree-Laws that have direct impact in the use of biomass (lignocellulosic) residues aimed at reforming the forest sector. These are based on three main areas of intervention: forest territorial planning and management, property ownership, and finally, forest fire prevention and firefighting.

The referred decree-laws are:

- Decree-Law no. 64/2017, of 12 June, defines the rules for construction and operation of power plants to produce bioenergy (electricity and heat) from forest biomass by municipalities;
- Decree-Law no. 65/2017, of 12 June, that updates the Legal Framework for Forest Management, Intervention, and Zoning Plans, approved by Decree-Law no. 16/2009, of 14 January, aiming at a better clarification of the relation between

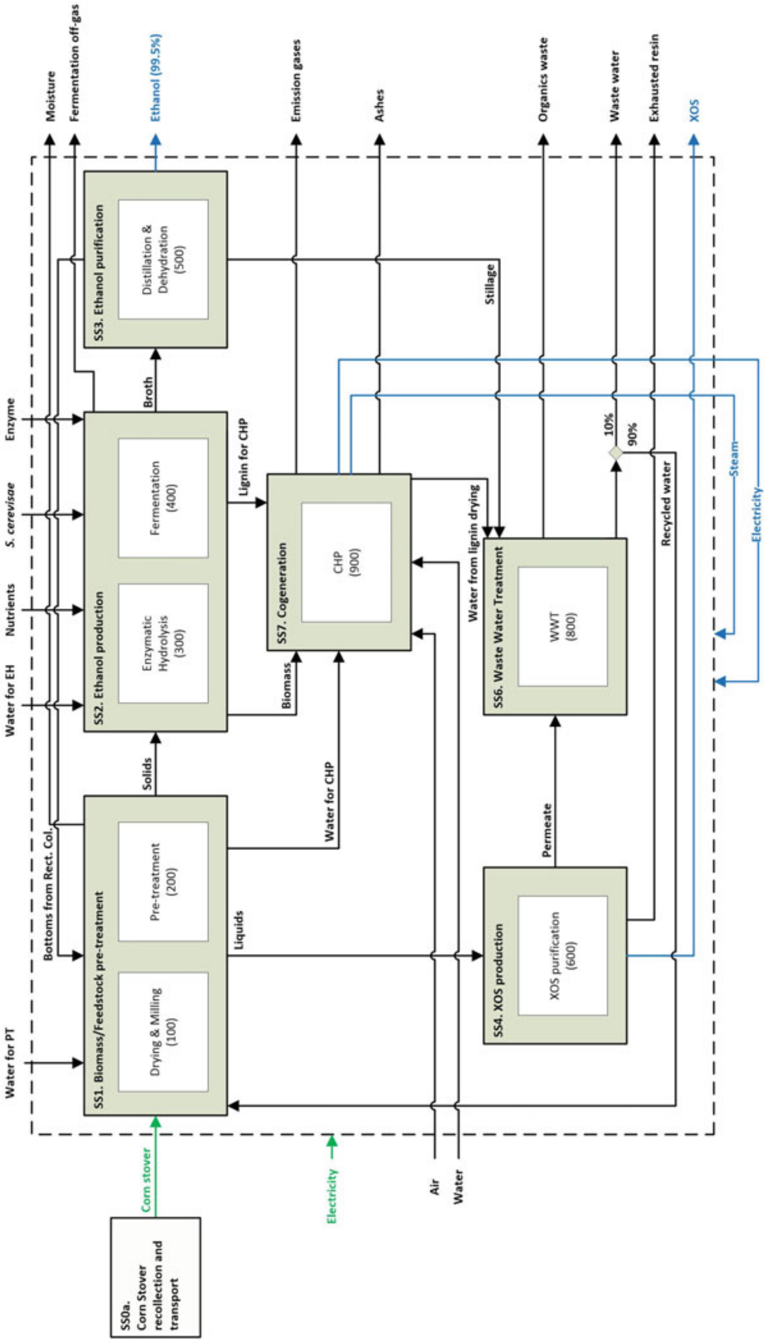

**Fig. 3.17** Simplified flowchart of the corn stover (only) biorefinery system

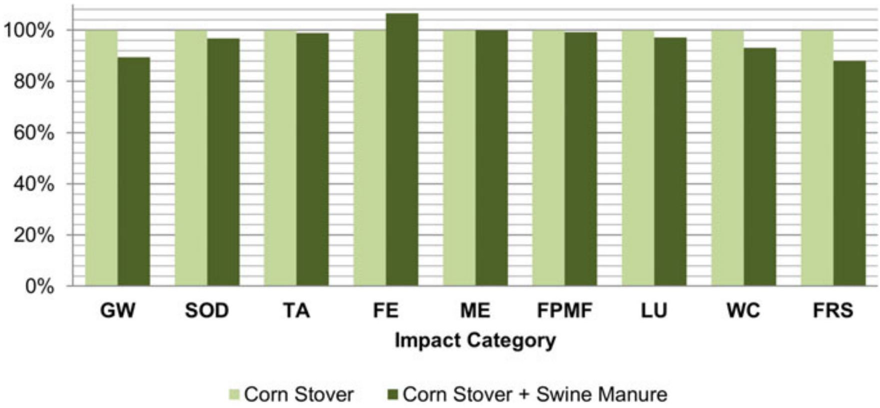

**Fig. 3.18** Evaluation of the effect on the impact categories when using swine manure in the corn stover biorefinery

the regional forest zoning programmes and other programmes and plans for territorial management and a stronger protection of the forests by providing the authority to monitor compliance with such rules to the Institute for Nature Conservation and Forests (Instituto da Conservação da Natureza e Florestas) ("ICNF") ('Decreto-Lei n.º 65/2017' 2017);

- Decree-Law no. 66/2017, of 12 June, that sets forth the conditions and procedure for the recognition of forest management entities (agricultural cooperatives, private limited-liability companies or public limited-liability companies), who shall manage forest areas belonging to several owners in order to enhance their profitability by means of joint management ('Decreto-Lei n.º 66/2017' 2017);
- Decree-Law no. 67/2017, of 12 June, that updates the rules for creating forest intervention areas (ZIFs), approved by Decree-Law no. 127/2005, of 5 August, as amended, as well as enhances the creation of new ZIFs and improves the operation of existing ones ('Decreto-Lei n.º 67/2017' 2017).

Furthermore, regarding biorefineries, the Resolution of Council of Ministers no. 163/2017 ('Resolução do Conselho de Ministros n.º 163/2017' 2017) adopted the National Plan for the Promotion of Biorefineries (PNPB), under a policy of valuing the renewable energy sources and in the context of the use of the biomass, in accordance with the existing national potential. A strategy with the 2030 horizon is assumed to promote all types of advanced biorefineries in the country from biomass, so far not valued, waste or low economic value, such as agricultural and forestry waste biomass.

In line with the assessment reported in this chapter, Portugal has biomass residues available throughout the continental territory, with potential to be used in biorefineries and for energy purposes (electricity, heat, and advanced biofuels). Specifically, corn residues still have an untapped potential for the biorefinery concept. The integrated biorefinery concept (LCB and ADB) is an example of the application of circular bioeconomy, as the generated compost from the anaerobic digestion of swine manure can be used as a fertilizer for the corn cultivation. Nonetheless, it is important to notice that corn cultivation is seasonal, therefore an integrated biorefinery which can process more than one type of lignocellulosic biomass is more advantageous. The availability of different type of biomass residues in a certain radius can directly affect the profitability of the biorefinery.

Still, based on the referred legislation, one can conclude that the implementation of a corn stover/swine manure integrated small-scale biorefinery is very realistic in the short term, not only in the Portuguese territory but also all across Europe where different lignocellulosic residues and wet residues are available.

## 3.7 Conclusions

Valorization of all lignocellulosic biomass fractions is of extreme importance for the economic and sustainable viability of a biorefinery. The hemicellulose fraction, if valorized into oligosaccharides, shall be a possible way for the breakthrough of lignocellulosic-based biorefineries and its implementation.

Small-scale biorefineries can be economically viable if adapted to rural areas with suitable logistics and supply chains. Similar conclusions have already been achieved for a similar process by (Lopes et al. 2019), but in which the main product of the fermentation would be isobutene (in addition to the XOS obtained in the pre-treatment). A heuristic approach to evaluate the possible technological routes and the selection of feasible scenarios, followed by a detailed techno-economic analysis together with process simulation tools are useful for scale-up analysis and economic viability of biorefineries. Small-scale biorefineries can be environmentally sustainable depending on the products obtained, and subsequently the required operation units, along the whole value chain.

In a near future, it will be important to assess other types of residual biomass to overcome the issues of seasonality and availability (e.g., eucalyptus residues). Also, Social Impact Assessment on the various stakeholders (e.g., local community, agricultural producers, livestock producers, workers, etc.) for the implementation of a biofuels/bioproducts based biorefinery shall be addressed.

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# Composition and Chemical Structure of Hemicelluloses and Polysaccharides with Capability of Gel Formation

# 4

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## Abstract

Considering the biorefinery point of view, hemicelluloses and gel-forming polysaccharides are crucial components of lignocellulosic biomass, due to their potential to form products of immense value as ingredients or additives, and are widely used and commercialized worldwide for manufacturing numerous products, mainly in the pharmaceutical, food, and cosmetic industries. Despite having similar uses, the chemical structure and composition of these polysaccharides differs. These differences may be due to their monomeric units, such as glucuronoxylan (formed by xylose units and methyl glucuronic acid residues) and glucomannan (formed by glucose and mannose units). In other cases, differences may be observed in the proportion or position of side groups such as kappa (κ-), iota (ι-), and lambda (λ-) carrageenan that have 1, 2, and 3 sulfate groups per disaccharide, respectively. These differences remarkably alter their properties, mechanisms, and application. This chapter focuses on understanding the different chemical structures and composition of hemicelluloses and gel-forming polysaccharides and their effects on these properties.

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M. Brienzo (ed.), *Hemicellulose Biorefinery: A Sustainable Solution for Value Addition to Bio-Based Products and Bioenergy*, Clean Energy Production Technologies, https://doi.org/10.1007/978-981-16-3682-0_4

**Keywords**

Hemiceluloses · Gel-forming polysaccharides · Chemical composition and structure

## 4.1 Introduction

The carbohydrates that constitute the plant cell wall are classified into three main groups: cellulose, hemicelluloses, and polysaccharides capable of forming gels. This classification is based on the ability of carbohydrates to extract these components from plant biomass. Polysaccharides capable of forming gels are successfully extracted using neutral aqueous solutions, whereas hemicellulose requires concentrated sodium or potassium hydroxide solutions; however, hemicelluloses are partially extractable in aqueous solutions, which can make the classification ambiguous. The fractionation of the material into polysaccharides capable of forming gels or/and hemicellulose (liquid fraction) and cellulose (solid fraction) allows it to be used as a raw material for producing bioproducts of commercial interest (Faik 2010; Gellerstedt et al. 2009). Examples of hemicellulosic fraction application include the production of oligosaccharides with prebiotic potential (example: xylooligosaccharides (XOS), market value expected to reach US$78.1 million by the end of 2025) (QY Research Reports 2019), feed additive (market value expected to reach US$13.4 billion by 2023) (The Business Research Company 2020), and low-calorie sugar production (example: xylitol, market value of US $883.5 million in 2019) (Ahuja and Mamtani 2019).

Moreover, pectin, xyloglucan, and carrageenan have gained immense interest among the polysaccharides capable of forming gels. These are mainly used as gelling agents, thickeners, emulsifiers, or stabilizers in the food industry (for manufacture of jams, jellies, dairy products, meat products, juices, and bakery) and in the pharmaceutical industry (personal care products, edible films, foams, and pharmaceuticals formulation). Pectin had an estimate market value of US$1 billion by 2019 (Markets and Markets 2019), whereas the global carrageenan market value worth was US $931.6 million in 2020 (Market Data Forecast 2020).

Furthermore, the previous literature reported that the name hemicellulose is used for polysaccharides extracted in the alkaline solution. This name was based on the assumption that these polysaccharides are hydrolyzed more easily than cellulose. In addition, the findings reveal that these polysaccharides extracted with alkaline solution represent a distinct and separate group of polysaccharides capable of forming gels. Thus, hemicellulose is distinguished from cellulose and polysaccharides capable of forming gels. Hemicelluloses and/or polysaccharides capable of forming gels are found on the cell wall of the plant in a *matrix* located between the cellulose fibrils (Ek et al. 2009). Noncellulosic polysaccharides, including hemicellulose and those capable of forming gels, are further discussed in this chapter.

## 4.2 Hemicelluloses

Hemicelluloses are one of the main components comprising 20–35% (dry basis) of plant biomass. Hemicelluloses, in general, can be classified into two main groups: glucomannans (main chain polysaccharide containing glucose and mannose, that is, heteropolysaccharide) and xylans (main chain polysaccharide containing xylose, that is, homopolysaccharide); however, remarkable differences are verified in the side groups of these hemicelluloses (absence and/or quantity), which increases the complexity in their classification, as summarized in Table 4.1 (Ek et al. 2009; Scheller and Ulvskov 2010).

Cellulose, hemicelluloses, and polysaccharides capable of forming gels are structural carbohydrates, as they form the support structure of the plant cell, that is, its cell wall. Hemicelluloses and polysaccharides capable of forming gels are found in a matrix between cellulose fibrils. The components of plant biomass are strongly associated and their separation is quite complex. Hemicelluloses are found in wood, grasses, cereals, and some primitive plants. The type and amount of hemicellulose varies widely, depending on the plant materials, tissue type, growth stage, growth conditions, storage, and extraction method.

### 4.2.1 Supramolecular Structure

The molecular structure of the native hemicellulose molecule indicates that it is not possible to form a crystalline structure due to the presence of irregularly arranged side groups (Table 4.1); however, under certain conditions, hemicellulose may crystallize, although these polymers are not considered crystalline in situ in the cell wall of plant biomass. The dorsal structure of the hemicelluloses in its crystalline form or in aqueous solution has a triple-left conformation, with a rotation of 120° for each xylose residue. The hemicellulose chains have an extension in their conformation, similar to a slowly twisted ribbon. In cellulose, the hydroxymethyl group at position 5 of the glucose ring participates in a cooperative network of intra- and intermolecular hydrogen bonds; however, hemicelluloses are unable to form such network, since they contain only two atoms of hydrogen at position 5. The presence of water is apparently necessary for hemicelluloses to acquire a stable and orderly structure; moreover, crystallization can occur after removing a portion of the side chains and/or some reduction in the chain length. The water molecules are incorporated between neighboring hemicellulose chains, wherein a column is formed along these chains. In an aqueous medium, cellulose fibrils interact with hemicellulose, resulting in a conformation of the unchecked hemicellulose molecule with the hydrated polysaccharide in isolation (Ek et al. 2009).

**Table 4.1** Main hemicelluloses found in dicotyledons (hardwood), monocotyledons (softwood), and grasses

| Source | Hemicelluloses | [a]Amount (%) | Units | | Bond type (GL) | Molar ratio (CP:GL)[c] | References |
|---|---|---|---|---|---|---|---|
| | | | Main chain (CP)[b] | Side groups (GL) | | | |
| Dicotyledonous wood | Arabinoglucuronoxylan | 15–35 | β-D-Xylp | 4-OMe-α-D-GlcpA | 1→2 | 10:1 | Ek et al. (2009) |
| | | | β-D-Xylp | α-L-Araf | 1→3 | 10:0.1 | |
| | | | β-D-Xylp | *O*-Acetyl | – | 10:7 | |
| | Glucomannan | 2–5 | β-D-Manp | *O*-Acetyl | – | 1–2:1 | Ek et al. (2009) |
| | | | β-D-Glcp | *O*-Acetyl | – | 1:1 | |
| Monocotyledonous wood | Galactoglucomannan | 5–8 | β-D-Manp | α-D-Galp | 1→6 | 3–4:1 | Ek et al. (2009) |
| | | | β-D-Glcp | α-D-Galp | 1→6 | 1:1 | |
| | | | β-D-Manp | *O*-Acetyl | – | 3–4:1 | |
| | | | β-D-Glcp | *O*-Acetyl | – | 1:1 | |
| | Glucomannan | 10–15 | β-D-Manp | α-D-Galp | 1→6 | 3–4:0.1 | Ek et al. (2009) |
| | | | β-D-Glcp | α-D-Galp | 1→6 | 1:0.1 | |
| | | | β-D-Manp | *O*-Acetyl | – | 3–4:1 | |
| | | | β-D-Glcp | *O*-Acetyl | – | 1:1 | |
| | Arabinoglucuronoxylan | 7–15 | β-D-Xylp | 4-*O*Me-α-D-GlcpA | 1→2 | 10:2 | Ek et al. (2009) |
| | | | β-D-Xylp | α-L-Araf | 1→3 | 10:1.3 | |
| Grasses | Arabinoglucuronoxylan | 15–30 | β-D-Xylp | 4-*O*Me-α-D-GlcpA | 1→2 | 10:1 | Scheller and Ulvskov (2010) |
| | | | β-D-Xylp | α-L-Araf | 1→3 | 10:1 | |
| | | | β-D-Xylp | Acetyl | – | 10:7 | |
| | Glucomannan | 0–2 | β-D-Manp | *O*-Acetyl | – | – | Scheller and Ulvskov (2010) |
| | | | β-D-Glcp | *O*-Acetyl | – | – | |

[a] Percentage data presented on a dry basis

[b] The main chain of all hemicelluloses is linked via a β-1→4 bond type

[c] Approximate data

### 4.2.2 Xylans

Xylans are a specific group of hemicelluloses. All xylans have a main chain comprising a structure containing β-(1,4)-D-xylopyranosyl residues (Fig. 4.1). The xylan molecule is essentially linear; however, different side groups connect the main chain of the molecule, as follows:

- 4-*O*-methyl-glucuronic acid (4-*O*Me-α-D-Glc*p*A, C2 containing alcoholic hydroxyl residues of β-(1,4)-D-xylopyranosyl (Xyl) connected to the $C_1$ of 4-*O*-methyl-glucuronic acid by ether α-(1,2) binding) (Faik 2010; Ek et al. 2009);
- α-L-arabinofuranose (L-Ara*f*) or arabinosyl group (C2 and/or C3 containing alcoholic hydroxyl residues of β-(1,4)-D-xylopyranosyl (Xyl) connected to the C1 of the arabinose molecule by an ether α-(1,2) or α-(1,3) bond type) (Faik 2010; Ek et al. 2009);
- *O*-acetyl (Ac) groups (C2 and/or C3 containing alcoholic hydroxyl residues of β-(1,4)-D-xylopyranosyl connected to the acid hydroxyl of the acetic acid molecule via ester-type bonding) (Faik 2010; Ek et al. 2009);

Xylans are the main components of hemicelluloses found in the secondary cell wall of plants, representing approximately 20–30% of the biomass in dicotyledonous plants (hardwood) and 15–35% of the biomass in monocotyledons (softwood) and grasses (dry weight (Table 4.1) (Faik 2010; Ek et al. 2009; Scheller and Ulvskov 2010).

Xylans can be classified into different groups, as mentioned below.

- Arabinoglucuronoxylan (dicotyledonous and grasses, representing about 15–35% of biomass, dry weight) has the following side groups: 4-*O*-methyl-glucuronic acid (4-*O*Me-α-D-Glc*p*A) linked to the C2 of β-(1,4)-D-xylopyranosyl residues (Xyl), arabinosyl groups (α-L-Ara*f*) linked at the C2 or C3 position of β-(1,4)-D-xylopyranosyl residues, and *O*-acetyl (Ac) groups in an average molar ratio of

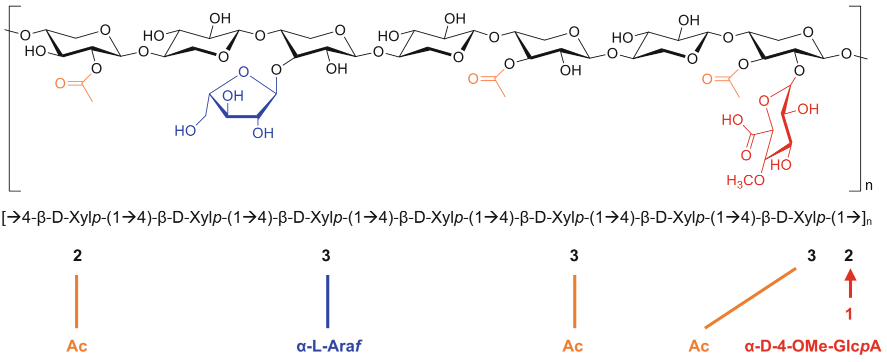


**Fig. 4.1** Schematic representation of the general structure of a xylan molecule. (Adapted from Gellerstedt et al. 2009)

10:1:0.1:7 (Xyl:AMeGlc:Araf:Ac), respectively (Table 4.1). Nevertheless, in case of grasses, the molar ratio of β-(1,4)-D-xylopyranosyl residues, 4-*O*-methyl-glucuronic acid, arabinosyl groups, and *O*-acetyl differ slightly, attaining a ratio of 10:1:1:7, respectively (Table 4.1). The average number of xylose units per arabinoglucuronoxylan molecule is about 84–108 (DPn); however, the variation in the xylose units in arabinoglucuronoxylan molecules is narrow, that is, it has a dispersity index ($M_w/M_n$) of approximately 1.1. The average molar mass ($M_w$ and $M_n$) of arabinoglucuronoxylan molecules varies considerably depending on the plant species, with an average value of 16,800 and 14,800 Da ($M_n$ and $M_w$, respectively), thereby providing a dispersity ($M_w/M_n$) of 1.13 (Faik 2010; Ek et al. 2009; Scheller and Ulvskov 2010).

- Arabinoglucuronoxylan (monocotyledons, on average represent 7–15% of the biomass, dry weight) has side groups 4-*O*-methyl-glucuronic acid (4-*O*Me-α-D-Glc*p*A) linked at the C2 position and arabinosyl groups (α-L-Ara*f*) connected at the C3 position of β-residues (1,4)-D-xylopyranosyl (Xyl), in an average molar ratio of 10:1.3:2 (Xyl:Araf:AMeGlc), respectively (Table 4.1); *O*-acetyl groups are not found in this case. The average number of xylose units per xylan molecule is about 90–120 (DPn). The average molar mass ($M_w$ and $M_n$) of arabinoglucuronoxylan molecules varies remarkably depending on the species of the plant, with an average value of 200,000 and 16,650 Da ($M_n$ and $M_w$, respectively) giving a dispersity index ($M_w/M_n$) of 1.20 (Faik 2010; Ek et al. 2009; Scheller and Ulvskov 2010).

### 4.2.3 Glucomannans

Glucomannans are another specific group of hemicelluloses. All glucomannans have a main chain comprising residues of β-(1,4)-D-mannopyranosil and β-(1,4)-D-glucopyranosyl linked through β-(1,4) glycosidic type bonds (Fig. 4.2) (Faik 2010; Ek et al. 2009; Scheller and Ulvskov 2010).

Glucomannans are one of the main components of hemicelluloses found in the secondary cell wall of plants, and may represent approximately 0–5% of the biomass (dry base) in dicotyledons and grasses and 10–15% of the biomass (dry weight) in monocotyledons (Table 4.1) (Faik 2010; Ek et al. 2009; Scheller and Ulvskov 2010).

In general, the molar ratio between β-(1,4)-D-mannopyranosil and β-(1,4)-D-glucopyranosyl residues varies from 1:1 to 1:4. In dicotyledons, the molar ratio between these residues is 1:1 and 1:2. Moreover, in certain cases, the mannosyl residues are connected to side groups comprising α-D-galactopyranosyl linked by α-D-(1–6) type bonds. In their native state, the alcoholic hydroxyls of β-(1,4)-D-mannopyranosyl residues of the glucomannan main chain are partially acetylated (C2 and/or C3 of the alcoholic hydroxyls of β-(1,4)-D-manopyranosil or β-(1,4)-D-glucopyranosyl residues linked to the acid hydroxyl of the acetic acid molecule via ester-type binding). *O*-acetyl groups are irregularly distributed along the main chain of the molecule (Table 4.1) (Ek et al. 2009).

Glucomananns can be classified into two different groups:

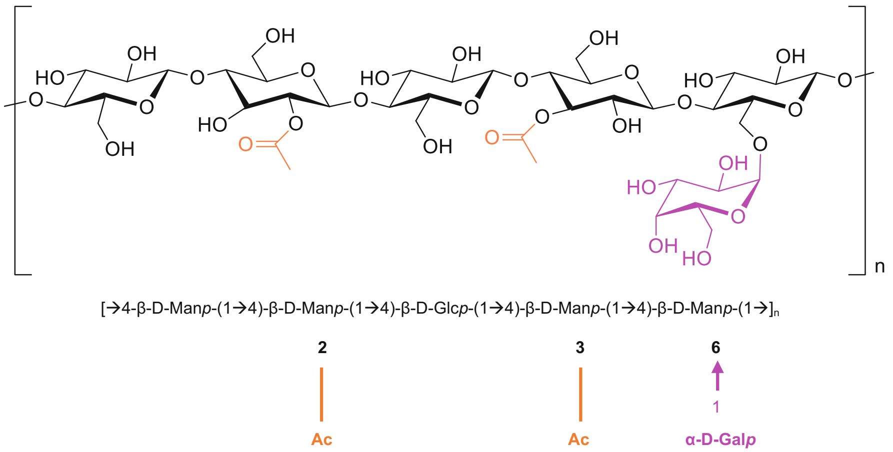


**Fig. 4.2** Schematic representation of the general structure of a glucomannan molecule. (Adapted from Ek et al. 2009)

- *Glucomannan* are acetylated along their main chain in a proportion of 1–4 residues of β-(1,4)-D-mannopyranosil or β-(1,4)-D-glucopyranosyl for each *O*-acetyl group. In addition, there is a rare side group of the α-(1,6)-D-galactopyranosyl type linked along the glucomannan main chain. It is found in dicotyledons and grasses (2–5% biomass, dry base, degree of polymerization of the order 60–70 (DPn)) and in monocotyledons (10–15% biomass, dry weight, degree of polymerization of the about 90–102 (DPn)) (Table 4.1) (Faik 2010; Ek et al. 2009; Scheller and Ulvskov 2010).
- *Galactoglucomannan* is Similar to glucomannan, however, it presents the side group α-(1,6)-D-galactopyranosil with greater frequency (1–4 residues of β-(1,4)-D-manopyranosil or β-(1,4)-D-glucopyranosil for each group α-(1,6)-D-galactopyranosyl) and 3–6 residues of β-(1,4)-D-manopyranosil or β-(1,4)-D-glucopyranosyl for each group of *O*-acetyl. It is found only in monocotyledons and comprises 5–8% of the biomass (dry weight) (Table 4.1). The higher frequency of degree of substitution with galactose units makes galactoglucomannan less soluble in water than glucomannan (Faik 2010; Ek et al. 2009; Scheller and Ulvskov 2010).

### 4.2.4 Hemicellulose–Lignin Complex

Lignin is an aromatic macromolecule comprising three main types of hydroxycinnamyl alcohols: *p*-cumaric, coniferyl, and synaphyl. When polymerized, these monolignols are denominated as monomeric units of lignin, as follows: *p*-hydroxyphenyl (H), guaiacyl (G), and syringyl (S). These monomer units are irregularly connected chemically to various ether-like bonds, the most common being arylglycerol-β-aryl (β-*O*-4′) (De Oliveira et al. 2017; Ek et al. 2009). In this

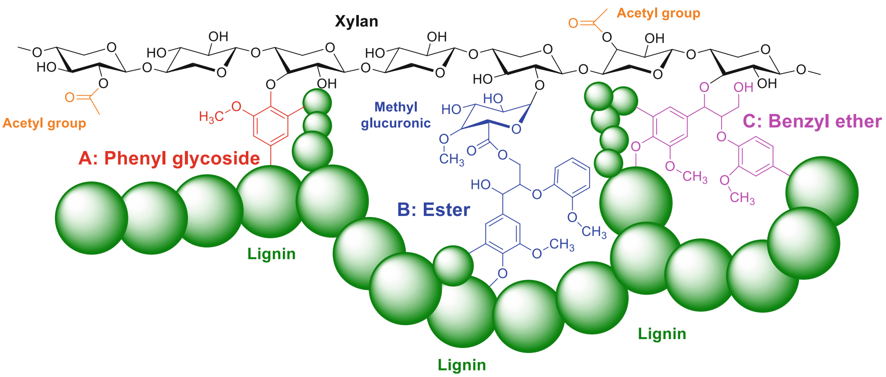


**Fig. 4.3** Main types of linkages between xylan and lignin in lignin–carbohydrate complex: (A) phenol glycoside, (B) ester, and (C) benzyl ether. (Adapted from Balakshin et al. 2007)

context, lignin molecules are chemically linked with hemicellulose molecules, that is, a lignin–carbohydrate complex is observed in the chemical structure of the plant cell wall; however, the present complex has an adverse chemical structure in the woods (dicotyledonous and monocotyledons) when compared to grasses.

The main chemical bonds between lignin and hemicellulose molecules in dicotyledons are illustrated in Fig. 4.3.

Figure 4.3 represents a xylan molecule, but similar chemical bonds between lignin and hemicellulose also occur in glucomannans; however, in this case the bonds are between mannose and/or glucose residues (Fig. 4.2).

The occurrence of these bonds was confirmed in lignin–carbohydrate complex isolated from *pine*wood (monocotyledon), via nuclear magnetic resonance (RMN-2D). Figure 4.3a–c illustrate a phenol glycoside bond, an ester-like bond, and a benzyl ether bond, respectively. In case of glycosidic phenol bond, the corresponding area in the spectrum has been integrated indicating that this bond is present in approximately 8 units for every 100 $C_9$ units of lignin, thus being the most frequent bond (Balakshin et al. 2007).

The main chemical bonds between lignin and hemicellulose molecules in grasses are illustrated in Fig. 4.4. Lignin in grasses is closely linked to xylan through ferulic and *p*-cumaric acids.

These phenolic acids are linked to the $C_5$ position of an arabinose molecule, via an ester bond. Arabinose is coupled to xylan via an ether bond (Hatfield et al. 1999; Jeffries 1990). Moreover, lignin is connected to phenolic acids through propanoic chains on α carbon, with mainly ether bonds. Phenolic acids are coupled to lignin via radical processes; however, ferulic and *p*-coumaric acids are only coupled to monomers (coniferyl and synaphyl alcohols) and not to lignin oligomers. The main function of these acids is to act as nucleation points during lignin biosynthesis in grasses (Hatfield et al. 1999). Masarin et al. (2011) reported that sugarcane bagasse has approximately 1.7% ferulic acid and 7% *p*-cumaric acid (w/w, dry basis).

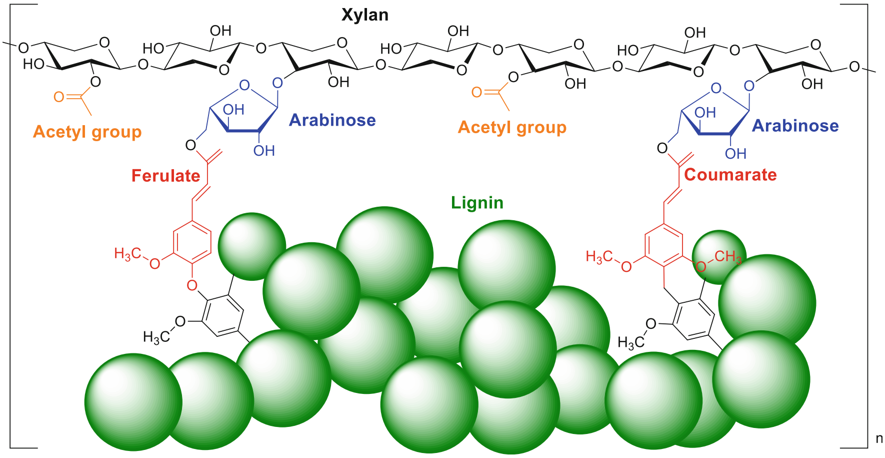


**Fig. 4.4** Scheme depicting ferulate and coumarate residues coupled to lignin; both residues of coniferyl and synapyl alcohols are linked with ferulates and coumarates. (Adapted from Hatfield et al. 1999)

## 4.3 Polysaccharides Capable of Forming Gels

The plant cell wall is formed by different types of polymers (cellulose, hemicellulose, lignin, pectin, xyloglucans, and others) that interact to form a barrier conferring protection to the cell (Agrios 2005). In plants, the primary and secondary cell wall can be identified; the first one surrounds the cells, allowing their growth and expansion, and the second one is formed when the cell has finished its development. The lamella media act as a link between different cells Vargas Garcia et al., (2014).

The different components constituting the plant tissues are not independent. Pectin and xyloglucan (XyG) are in the primary cell wall and in the middle lamina (Hayashi and Kaida 2011; Yapo et al. 2007). Studies point to the existence of a high degree of interaction between cellulose and xyloglucan, which is represented in some accepted drawings on the tied network model of the primary cell wall (McCann et al. 1990; Pauly et al. 1999). However, the biomechanical evidence that supports the interactions between xyloglucan and cellulose is indirect and open to different interpretations (Park and Cosgrove 2012), especially since there are some nuclear magnetic resonance (NMR) studies that have not detected a great interaction between these two polysaccharides (Bootten et al. 2004; Dick-Pérez et al. 2011; Park and Cosgrove 2012).

Furthermore, pectin binds to cellulose in vitro as observed via NMR studies (Dick-Pérez et al. 2011; Thompson and Stephen 2000; Zykwinska et al. 2005). In addition, Popper and Fry (2005, 2008) suggested that XyG and pectin are linked, and approximately, 30–70% of the total XyG are covalent linked to pectin as observed in the in vitro study using various angiosperm cell-suspension cultures (arabidopsis, sycamore, rose, tomato, spinach, maize, and barley).

For polysaccharides capable of forming gels, their technological performance as emulsifiers needs to be explored, as they can be used for structuring of food or hard-shelled capsule while replacing gelatin or synthetic surfactants (Alba and Kontogiorgos 2017).

### 4.3.1 Pectic Substances and Pectin

Pectic substances, according to the American Chemistry Society, are classified into four main groups (Álvarez García 2018).

- *Protopectin*: this is present in immature fruits, and is insoluble in water. When hydrolyzed, it produces pectin or pectic acids.
- *Pectin or polymethyl galacturonate*: When the number of carboxyl groups esterified with methanol of the galacturonated units are higher than 75%.
- *Pectinic acids*: When the content of methylated galacturonate units is lower than 75% of the polygalacturonan chain.
- *Pectic acid:* This is a water soluble galacturan polymer, containing low amount of methoxyl groups.

#### 4.3.1.1 Pectin Structure

The pectin structure is defined as a complex non-starch and non-hemicellulose polysaccharides comprising mainly a backbone of D-galacturonic acid units (GalA) that are linked to each other with 1,4-glycosidic bond; according to Voragen et al., 2009, the main domain of pectin is denominated homogalacturonan (HG) (Fig. 4.5), which comprises 72–100 GalA units, and it could represent almost 60% of the total citrus pectin (Yapo et al. 2007).

The HG can be randomly acetylated at the C2 and/or C3 positions and methylated at C6 (Fig. 4.5); this fraction is characterized as *smooth region* that can rarely be interrupted by the hairy regions or rhamnogalacturonans (RG), wherein the side chains comprise various neutral sugars (Bonnin et al. 2002; Míguez et al. 2016).

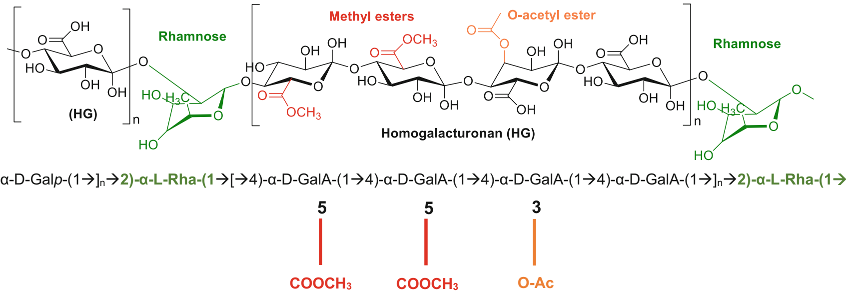


**Fig. 4.5** Structure of homogalacturonan (HG). (Adapted from Navarro-Garcia and Navarro-Garcia 1985)

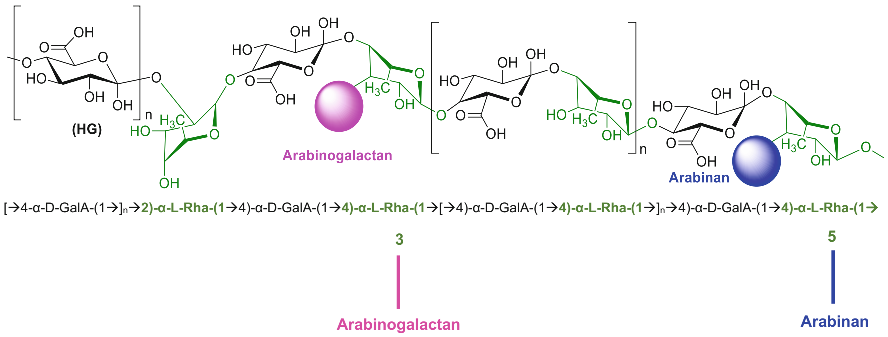


**Fig. 4.6** Schematic representation of the pectin structure (rhamnogalacturonan I, RG-I). (Adapted from Ridley et al. 2001)

According to Radenkovs et al. (2018), the degree of acetylation and methylation vary according to the origin and maturity stage of the plant. Moreover, the HG can present modifications such as neutralization by sodium, potassium, or ammonium (Jayani et al. 2005).

L-Rhamnose is a neutral sugar, which contributes to the main pectin chain formation, and it links (1–2) and (1–4) units to the galacturonate units and causes deviations of 90° in the axis of the chain (Navarro-Garcia and Navarro-Garcia 1985). L-Rhamnose represents approximately 2–4% of pectin (Jayani et al. 2005) and could be present in an alternation of galacturonic acid (Fig. 4.5) sequences of approximately 10–20 units (Navarro-Garcia and Navarro-Garcia 1985; Zhan et al. 1998).

The insertion of L-rhamnose allows identification of the second domain of pectin, that is, type I (RG-I) and type II (RG-II). The RG-I constitutes up to 20–35% of the total pectin (Mohnen et al. 2008). The specific structure of RG-I varies depending on the environment, tissue, and developmental stages of the plants (Ridley et al. 2001). In general, RG-I comprises repeating diglycosyl [α-(1,2)-D-GalA-α-(1,4)-L-Rha]*n* (Fig. 4.6), partly substituted at C4 (mainly) and/or C3 positions of α-L-rhamnose residues with single neutral glycosyl residues and polymeric side chains of different types namely arabinans, galactans, arabinogalactan I and II, and possibly galactoarabinans (Ridley et al. 2001).

In contrast, rhamnogalacturonan II (RG-II) has low molecular weight (5–10 kDa) (Yapo et al. 2007). The structure of RG-II is complex, and comprises at least eight 1,4-linked α-D-GalpA units with four different of side chains (Fig. 4.7) (Yapo et al. 2007).

The RG-II comprises 12 different types of glycosyl residues, including apiose, 2-*O*-methyl xylose, 2-*O*-methyl fucose, 3-C-carboxy-5-deoxy-L-xylose (acetic acid), 3-deoxy-D-lyxo heptulosaric acid (Dha), and 2-keto-3-deoxy-D-manno octulosonic acid (Kdo) (Ridley et al. 2001; York et al. 1986). Another domain of pectin is the xylogalacturonan (XG), which comprises an HG backbone that it is substituted with single β-1,3-xylose residues or such residues substituted with a few additional xylose

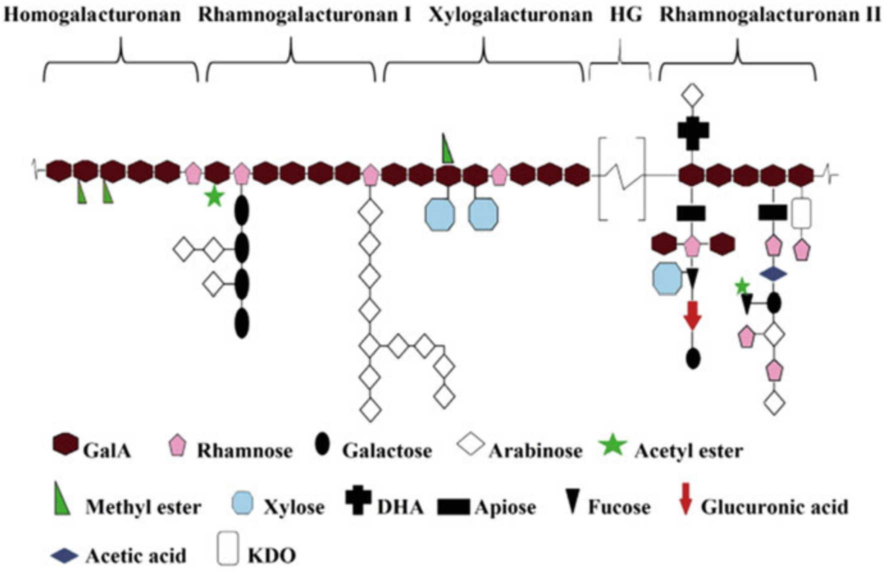


**Fig. 4.7** Schematic representation of the pectin structure (rhamnogalacturonan II, RG-II). (Retrieved from Míguez et al. 2016 and Radenkovs et al. 2018)

residues (Jensen et al. 2008) (Fig. 4.7). The degree of xylosidation may vary according to the source (Radenkovs et al. 2018).

#### 4.3.1.2 Chemical Characteristics and Their Effects on Emulsifying Pectin Capacity

In general, tissue pectin's range from 60% to 90% degree of esterification (DEs) (Sundar et al. 2012). According to these Des, pectin can be classified as HM-pectins and LM-pectins. The commercial HM-pectin typically has a DE range from 60% to 75%, whereas LM-pectins could have a range from 20% to 40% (Sundar et al. 2012). The methyl-esterification of linear HG units could vary in quantity and distribution of methyl groups on the HG backbone (Alba and Kontogiorgos 2017). The high methoxyl pectin forms gels when heated in acid solutions with a low pH (2–4) and in the presence of high sugar concentrations (55–75%). Low methoxyl pectin can form a gel in a wide range of pH (2–6) with or without limited sugar in the presence of divalent ions such as calcium ($Ca^{2+}$) (Sundar et al. 2012).

Similar to most polysaccharides, pectin is generally not considered to be an emulsifying agent (Akhtar et al. 2002); however, its structure may enhance emulsification; for example, a previous study reported that molecular weight was more important in enhancing emulsification than the DE value (Akhtar et al. 2002; Schmidt et al. 2017). Moreover, another research revealed that higher DE (>80%) results in reduced emulsion droplet sizes and improved long-term emulsion stability (Schmidt et al. 2015a). In contrast, another study reported that even a minimum quantity of acetyl groups (10%), which are similar to ferulic acid, may remarkably enhance the emulsifying properties of pectin, particularly at low protein contents (Alba and Kontogiorgos 2017; Chen et al. 2016).

Furthermore, the proteinaceous moieties present in pectin could reduce the interfacial tension in an emulsion acting as anchors that facilitate adsorption of pectin chain at the interface (Alba and Kontogiorgos 2017). The sugar beet and okra pectin reveal higher protein content than citrus apple pectin (Alba and Kontogiorgos 2017). A previous study on sugar beet pectin reported that the use of protease and arabinose/galactanase reduced the emulsifying properties of pectin, which highlights the importance of protein and lateral chain of pectin (Funami et al. 2011).

The sugar beet pectin has poor gelling properties due to its greater sugar content and its highest degree of acetylation; however, it presents good emulsifying properties (Guo et al. 2018; Chen et al. 2016; Funami et al. 2011). Another study reported that a covalent link can be created through the Maillard reaction between reducing carbohydrates of sugar beet pectin and the free amino group of a whey protein isolate; this conjugation decreases the interfacial tension and allows to improve the emulsifying properties in protein preparation (Guo et al. 2018).

#### 4.3.1.3 Sources of Pectin and Extraction Method

The main sources for commercial pectin production are citrus peels, apple pomace, and sugar beet pulp. The extraction of pectin with conventional techniques requires sulfuric, nitric, phosphoric, acetic, or hydrochloric acid; however, due to environmental concerns, organic acids such as citric acid and acetic acid have gained immense interest (Yang et al. 2018). Other methods that can be used in extracting pectin include ultrasound assisted-extraction, microwave-assisted extraction, and enzyme-assisted extraction (EAE). According to Marić et al. (2018), to extract the maximum pectin yield with the highest quality, it is necessary to optimize and standardize the specific methods according to the target plant materials (food waste and by-products), since the extraction process can modify the functional, physicochemical and technological properties, as well as the possible applications of pectin (Alba and Kontogiorgos 2017). Table 4.2 summarizes few characteristics of different pectin sources.

### 4.3.2 Xyloglucan

Xyloglucan is a mucoadhesive polysaccharide extracted from the cell wall of vascular plants. It is found in the gelatinous layer of the cell wall, middle lamellae, and in the primary cell walls of higher plants, where it interconnects with cellulose microfibrils (Dutta et al. 2020). Xyloglucan (XG) is present in various species including *Hymenaea courbaril*, *Salvia hispanica*, *Guibourtia thymenaefolia*, *Detarium senegalense*, *Copaifera langsdorffii,* and *Tamarindus indica*. Among these, xyloglucan obtained from tamarind seed has more commercial importance (Han et al. 2020).

**Table 4.2** Chemical characteristics and extraction yield of various pectins

| Plant | Source of pectin isolation | Yield of pectin recovery (%) | GalA[a] (%) | DE[a] (%) | MW[a] (kDa) | DAc[a] (%) | Protein (%) | Neutral monosaccharide (%) | References |
|---|---|---|---|---|---|---|---|---|---|
| Citrus pectin | Lime peel | 13.4–26.3 | 91.6 | 82.2 | 342.7 | 2.5 | 1.9 | **Ara:** 1.3–9.3 | Naghshineh et al. (2013), Dominiak et al. (2014) |
| | Mandarin orange peel | 21.95 | 68.9 | | | | 2.8 | **Fuc:** 0.1–0.16 | Wang et al. (2014) |
| | Orange peel | 24.2 | | | | | | **Gal:** 1.6–4.1 | Boukroufa et al. (2015) |
| | Sour orange peel | 29.1 | | 35.5 | | | | **Glc:** 0.8–3.3 | Hosseini et al. (2016) |
| | Pomelo peel | 23 | | 71.1 | 84.3 | | | **Rha**: 0.6–1.5 | Methacanon et al. (2014) |
| | Citrus | | | 70 | 73 | | | **Xyl:** 0.2–0.7 | Schmidt et al. (2015a, b) |
| Apple pomance | Apple pomace | 14.55–18.79 | 59.5–67.1 | 71 | 81 | 0.3–1.2 | 1.1 | ~30 | Kumar and Chauhan (2010) |
| | Royal pectin | | | 22.2–52.5 | | | | | Wikiera et al. (2015) |
| Sugar beet pulp | Sugar beet pectin | 23 | 65.9–72.4 | 55.2 | 311 | 26.74 | 1.5–4.5 | **Ara:** 2.6–10.8 | Li et al. (2015), Chen et al. (2015) |
| | | | | | | | | **Gal:** 1.6–8.5 | |
| | | | | | | | | **Glc:** 0.5–1.2 | |
| | | | | | | | | **Rha**: 0.6–3.1 | |
| | | | | | | | | **Xyl:** 0.3–0.6 | |
| | | | | | | | | **Fuc:** 0.3 | |
| | | | | | | | | **Man:** 0.05 | |

[a] *GalA* galacturonic acid, *De* degree of esterification, $M_W$ molecular weight, *DAc* degree of acetylation. (Retrieved and adapted from Dranca and Oroian 2018)

Xyloglucan is an important polysaccharide of the primary cell wall that is covalently bound to cellulose, and coats and joins adjacent cellulose microfibrils, forming a wall support network. The remodeling of this network by the expansions, cellulases, xyloglucanases, and xyloglucan transglycosylases, is presumed to be crucial in wall softening, further leading to cell growth (Zhang et al. 2020).

In water and salt, XG forms a viscous fluid. It is commonly employed in the food industry as an emulsifier, thickener, and emulsion stabilizer. It is biocompatible, biodegradable, and nontoxic in nature (Sakakibara et al. 2019). It is approved by the Food and Drug Administration (FDA) for use as a food additive, stabilizer, and thickening agent or gelling agent.

Xyloglucan polysaccharides are made up of heptasaccharide, nanosaccharide, and octasaccharide units. The side chains of xyloglucan comprise numerous galactose units (Fig. 4.8) (Han et al. 2020).

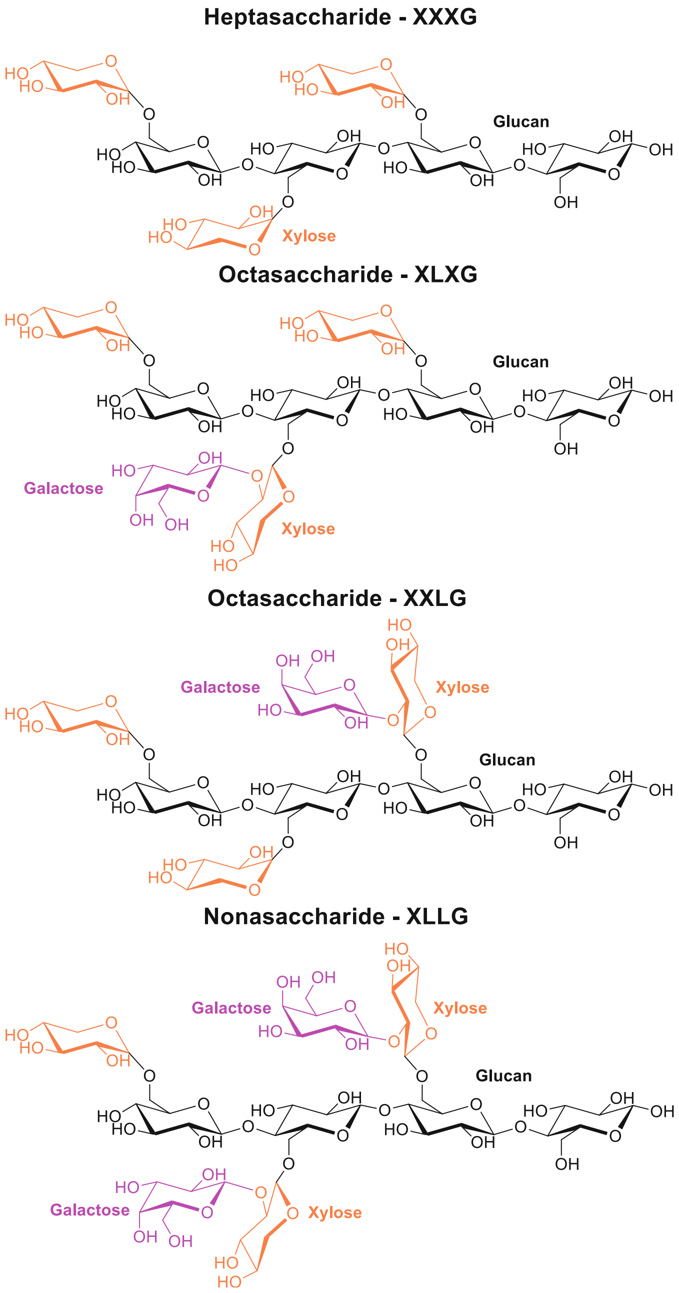
Glucose, galactose, and xylose are present in xyloglucan as monomers in different molar ratios according to their origin. The average molecular weight of xyloglucan is 50,000 Da. The chemical structure and characteristics of xyloglucan are summarized in Fig. 4.8 and Table 4.3.

### 4.3.3 Carrageenan

Carrageenan is the general name for a family of high molecular weight sulfated polysaccharides, formed by alternate units of D-galactose and 3,6-anhydro-galactose joined by α-1,3 e β-1,4 glycosidic linkage (Necas and Bartosikova 2013; Zia et al. 2017). It can be obtained by conventional (maceration, percolation, Soxhlet) or nonconventional (pressurized liquid extraction, subcritical water extraction, supercritical fluid extraction, microwave-assisted extraction, and ultrasound-assisted extraction) methods. Even though nonconventional methods are aligned with the biorefinery concept, conventional methods are mostly used in the industry worldwide (Rudke et al. 2020).

Red seaweed (*Rhodophyta*) is the main source of carrageenan. At industrial scale, carrageenan is obtained from *Kappaphycus alvarezii* (Masarin et al. 2016; Paz-Cedeno et al. 2019; Roldán et al. 2017; Solorzano-Chavez et al. 2019), *Eucheuma denticulatum* (Buriyo et al. 2001; Funami et al. 2007; Viana et al. 2004), *Chondrus crispus* (McCandless et al. 1973; Villanueva et al. 2009), and *Sarcothalia crispate* (Hughes et al. 2018) (Table 4.4), wherein *Kappaphycus* and *Eucheuma* seaweeds cultivated in Indonesia and Philippines are responsible for approximately 90% of carrageenan production (Campbell and Hotchkiss 2017; Naseri et al. 2019).

Abundant production for export markets has been achieved in Madagascar, United Republic of Tanzania, Malaysia and Zanzibar. In countries such as East Timor, Cambodia, Vietnam, Myanmar, China, Mozambique, Kenia, Argentina, Colombia, Panama, Peru, Brazil, Ecuador, Venezuela, and Mexico, the commercial production of carrageenan is increasing (Campbell and Hotchkiss 2017). Among seaweed-derived polysaccharides, the carrageenan market is the largest and most


Heptasaccharide - XXXG

Octasaccharide - XLXG

Octasaccharide - XXLG

Nonasaccharide - XLLG

**Fig. 4.8** Structure of xyloglucan. Black, glucose; orange, xylose; pink, galactose. (Adapted from Han et al. 2020)

**Table 4.3** General characteristics of the xyloglucan molecule

| Source | Characteristic features | References |
|---|---|---|
| *Hymenaea courbaril* | • Xyloglucan was efficiently extracted with 0.1 M NaCl, followed by ethanol precipitation (yield = 72% ± 5% w/w). | Arruda et al. (2015), Buckeridge et al. (1997), Busato et al. (2009), Sakakibara et al. (2019) |
| | • NMR spectra confirmed a central backbone composed by 4-linked glucose units partially branched at position 6 with nonreducing terminal units of xylose or galactose-(1→2)-xylose disaccharides. | |
| | • The solutions behave as a viscoelastic fluid. | |
| | • The polysaccharide did not reveal remarkable antibacterial or hemolytic activities. | |
| | • The native polysaccharide contained glucose, xylose, and galactose in *a* ~4.0:2.7:1 molar ratio. | |
| | • The influence of $Na_2SO_4$ as a kosmotropic salt on thermogelation. | |
| | • Treatment with a pure xyloglucan oligosaccharide-specific α-xylosidase, and a pure β-glucosidase; these structures were deduced to be XXXG and a new oligosaccharide XXXXG. | |
| *Detarium senegalense* | • Comprising a cellulosic backbone with single-unit, α-D-xylopyranosyl substituents attached to carbon-6 of the glucosyl residues, and few xylose residues further substituted at carbon-2 by β-D-galactopyranosyl residues. | Wang et al. (1996, 1997) |
| | • The main monosaccharide residues of the extract were glucose, xylose, and galactose in the ratio of 1.39:1.00:0.52, suggesting structural similarity to the xyloglucan group of cell wall storage polysaccharides. | |
| *Guibourtia hymenifolia* | • Seeds in 54.2% yield (w/w). The Glc:Xyl:Gal molar ratio was 3.3:2.3:1. | Lucyszyn et al. (2011) |
| *Copaifera langsdorffii* | • Germinating seeds of *Copaifera langsdorffii* are degraded by the action of β-galactosidase, endo-β-glucanase, α-xylosidase, and β-glucosidase, producing free galactose, glucose, and xylose. | De Alcântara et al. (1999) |
| *Tamarindus indica* | • Comprising glucose, xylose, and galactose ratio of 1.41:1.31:1, respectively. | Do Rosário et al. (2011), Pal et al. (2020), Santos et al. (2019), Zhang et al. (2020) |

(continued)

**Table 4.3** (continued)

| Source | Characteristic features | References |
|---|---|---|
| | • Comprising glucose, xylose, and galactose in a molar ratio of 3.1:1.7:1.0. | |
| | • Fractions revealed similar monosaccharide composition with Glc:Xyl:Gal molar ratios of 2.4:1.5:1.0, 3.8:1.5:1.0, and 3.6:2.4:1.0 for XGC, XGJ, and XGT, respectively. | |
| | • Main chain consisting of β-1,4-connected glucose molecules together with xylose (α-1,6) and galactose. | |

**Table 4.4** Sources of different types of carrageenan

| Carrageenan type | Source | References |
|---|---|---|
| Lambda (λ) | *Gigartina skottsbergii* | Doyle et al. (2010), Guibet et al. (2006), Saluri and Tuvikene (2020) |
| | *Chondrus ocellatus* | Zhou et al. (2004, 2006a, b) |
| Kappa (κ) | *Kappaphycus alvarezii* | Das et al. (2016), Gereniu et al. (2018), Masarin et al. (2016), Paz-Cedeno et al. (2019), Roldán et al. (2017), Solorzano-Chavez et al. (2019) |
| Iota (ι) | *Eucheuma denticularum* | Buriyo et al. (2001), Funami et al. (2007), Viana et al. (2004) |
| | *Meristiella gelidium* | Tischer et al. (2006) |
| Kappa (κ)/iota (ι) hybrid | *Mastocarpus pacificus* | Kravchenko et al. (2020) |
| | *Mastocarpus stellatus* | Azevedo et al. (2013), Barral-Martínez et al. (2020), Hilliou et al. (2006) |
| | *Sarcothalia crispate* | Hughes et al. (2018) |
| | *Gigartina skottsbergii* | Hughes et al. (2018) |
| | *Chondrus crispus* | Villanueva et al. (2009) |

important, with a projected average growth of ≈ 3% per year (CAGR). Presently, the global production capacity of carrageenan ranges from 80,000 MT year$^{-1}$ to over 100,000 MT year$^{-1}$ (Campbell and Hotchkiss 2017). Future Marker Insights (2017) estimate that the carrageenan market would approach US $1 billion by 2024.

The gelling, thickening, and emulsifying properties of carrageenan make it an important ingredient in food preparation, pharmaceutical applications, and experimental medicine (Necas and Bartosikova 2013). In the food industry, carrageenan is used to produce ice cream, meat and poultry, dairy products, drinks, and water-bases jellies (Hotchkiss et al. 2016). Moreover, several studies using carrageenan as immobilization support for enzymes and whole cell systems have been reported, aiming to produce vinegar (Osuga et al. 1984; Tosa and Shibatani 1995), fermented milk products (Sodini et al. 1997a, b), beer (Mensour et al. 1996, 1997), and ethanol (Krishnan et al. 1999; Nigam 2000; Norton et al. 1995).

#### 4.3.3.1 Structure

Carrageenan is a linear molecule, comprising repeated disaccharide units formed by D-galactopyranose and 3,6-anhydro-α-D-galactopyranose, joined alternatively by α-1,3 e β-1,4 glycosidic linkage, and contains approximately 15–40% of ester-sulfate groups with an average relative molecular mass above 100 kDa. It can be classified based on its solubility in potassium chloride and is traditionally identified by a Greek prefix: Lambda (λ), Kappa (κ), Iota (ι), Nu (ν), and Mu (μ) (Fig. 4.9). The μ- and ν- are the precursors of κ- and ι-carrageenan, respectively. Sulfate groups vary among carrageenan, with κ-, ι-, and λ- having one, two, and three units per disaccharide, respectively, resulting in 20%, 33%, and 41% of calculated sulfate content (w/w) (Campo et al. 2009; Jiao et al. 2011). Higher content of sulfate groups indicates higher solubility and lower gel strength.

κ-Carrageenan is formed by an alternating 3-linked β-D-galactose 4-sulfate and 4-linked anhydro-galactose units, and the only structural difference compared to the

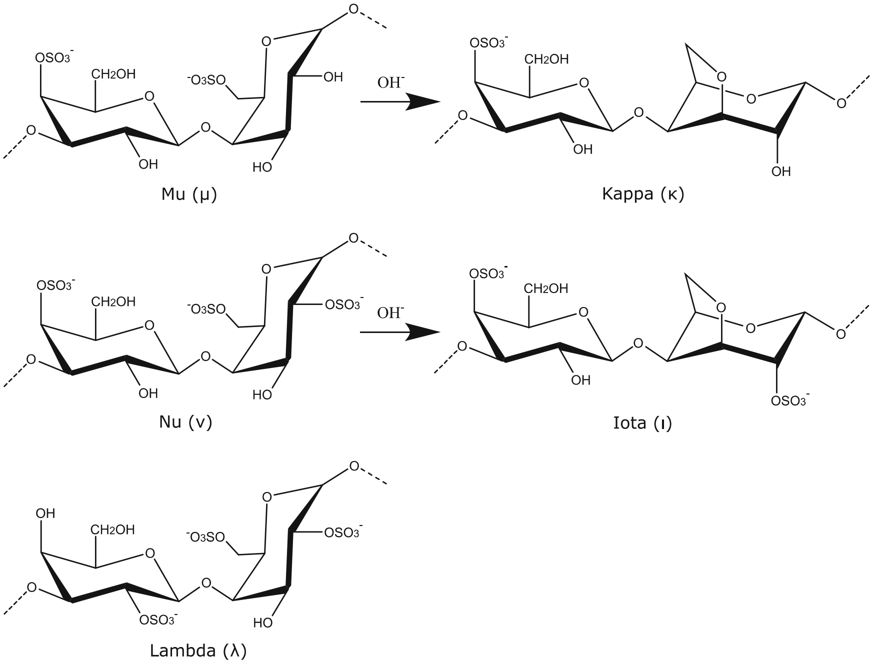


**Fig. 4.9** Chemical structure of the repeating disaccharide units of Mu (μ), Kappa (κ), Nu (ν), Iota (ι), and Lambda (λ) carrageenan

ι-carrageenan is that the latter has an additional sulfate group on C2 of anhydrogalactose residue. In contrast, λ-carrageenan is structurally more similar to *ν*-carrageenan (precursor of ι-carrageenan), with the only difference that the sulfate group in the galactose residue of λ-carrageenan is in C2 and not in C4 (Fig. 4.9).

Besides sulfate groups, *o*-methyl groups occurring in *κ*-carrageenan extracted from *Kappaphycus alvarezii* have been reported (Campo et al. 2009). In *λ*-carrageenan, pyruvate groups are also found forming a cyclic acetal at the positions 4 and 6 of 3-linked-galactose units (Chiovitti et al. 1998). Xylose residues in small amounts have been reported in carrageenan, but their location has not been determined (Van de Velde et al. 2002).

## 4.4 Conclusion

An understanding of the composition and structure of hemicelluloses and gel-forming polysaccharides is essential for the use of these components within the context of biorefineries. Among the hemicelluloses, we can differentiate two large groups, glucomannan and xylan. The main difference between these groups is in their main chain. In the case of glucomannan, they are heteropolysaccharides made up of glucose and mannose, while in the case of xylan, their main chain is only made up of xylose, being a homopolysaccharide. Both glucomannan and xylan have side groups that give them different properties (solubility, gelling capacity, dispersibility index). These groups are found in different amounts (or are sometimes absent) depending on the source. The main side groups are arabinosyl, galactose, acetyl, methyl glucuronic acid. In grasses, these groups enable the formation of the lignin-hemicellulose complex, functioning as a bridge between the xylan main chain and the lignin molecule. In the case of dicotyledonous plants, the link is directly between lignin and xylose residues.

On the other hand, the main gel-forming polysaccharides are pectin (and pectic substances), xyloglucan, and carrageenan. Pectin is mostly found in fruits and its structure is formed by a main chain of D-galacturonic acid units that is randomly esterified (acetylated and methylated) and is interrupted by rhamnose residues. The degree of esterification of pectin can influence gel formation and improve emulsification ability. Xyloglucan, generally used as an emulsifier, is generally found in the cell wall of vascular plants and its structure consists of a glucose chain with xylose and/or galactose side groups in different molar ratios. Carrageenan on the other hand is found in macroalgae, especially red algae (Rhodophyta), and it structure consists of a chain of D-galactopyranse and 3,6-anhydro-α-D-galactopyranose containing approximately 15–40% of ester-sulfate groups. A high content of sulfate in its structure leads to higher solubility and lower gel strength.

Finally, as can be seen, the structure and chemical composition of hemicelluloses and gelling polysaccharides differ greatly, so they must be carefully verified and studied when designing processes in a biorefinery context, in order to make the most of these components and obtain products of commercial interest.

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# Analytical Techniques Applied to Hemicellulose Structure and Functional Characterization

# 5

Ranieri Bueno Melati, Caroline de Freitas, and Michel Brienzo

## Abstract

The hemicelluloses compose the second most abundant renewable polysaccharide on the planet, only behind cellulose. They are classified as chemically heterogeneous polysaccharides, presenting a large proportion and content variation depending on the species, type of tissue, stage of growth, and environmental and physiological conditions, being constituted by around 80–200 units of sugar residues with low molecular mass. Among many biotechnological applications, hemicelluloses can be employed in the areas of energy, pharmaceutical products, and the food industry. In face of so many possible applications, it is possible to imagine that this material would be widely employed in the industry, however, that is not a reality. One of the factors that contribute to this scenery is the absence of analytical techniques that aim at the functional and structural characterization of this material. A deep comprehension of hemicelluloses physical-chemical properties and methods of analytical characterization of these properties is essential to project and operate plants for raw material conversion into refined products. The present chapter has the objective of presenting an abundant review of the physical-chemical techniques used to characterize xylans.

## Keywords

Hemicellulose composition · Hemicellulose function · Xylooligosaccharides · Physicochemical properties · Bioactivity · Antioxidant activity

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M. Brienzo (ed.), *Hemicellulose Biorefinery: A Sustainable Solution for Value Addition to Bio-Based Products and Bioenergy*, Clean Energy Production Technologies, https://doi.org/10.1007/978-981-16-3682-0_5

## 5.1 Introduction

Hemicelluloses are complex polysaccharides constituents in the plant cell wall, intimate organized with cellulose and lignin. Unlike cellulose, hemicelluloses are not homogeneous but polymers that consist of various sugar units, arranged in different proportions and with different/several substituents. Hemicelluloses are closely associated with cellulose by hydrogen bonds and are linked to lignin by covalent bonds (mainly α-benzyl ether linkages) (Peng 2009). Hemicelluloses are useful to produce gels, films, coatings, adhesives, gelling, stabilizing, and viscosity-enhancing additives in food and pharmacy (Abe et al. 2021; Freitas et al. 2021; Ebringerová 2005). Hemicellulose depolymerization can result in fermentable sugars, and ethanol can be produced by bioconversion. Therefore, understanding the chemical compositions and structural characteristics of hemicelluloses is useful to improve its industrial applications.

Different hemicellulose composition, structure, and amounts could be obtained according to biomass sources. In fact, hemicelluloses are a combination of different carbohydrate polymers, which primarily comprise different sugar residues including pentoses (β-D-xylose, α-Larabinose), hexoses (β-D-mannose, β-D-glucose, α-D-galactose), and/or uronic acids (α-D glucuronic, α-D-4-*O*-methylgalacturonic and α-D-galacturonic acids). In hardwoods, the major hemicellulose component is *O*-acetyl-4-*O*-methyl-glucuronoxylan, in which one-tenth of the xylopyranose backbone units are substituted at C-2 with α(1→2)-linked 4-*O* methylglucuronic acid residues, whereas a hydroxyl group is acetylated at C-2 or C-3 in about 70% of the xylopyranose backbone (Sunna and Antranikian 1997). However, in grasses, including switchgrass, arabinoxylan is the predominant component of hemicellulose. The hemicellulose consists of β-(1→4) linked xylose units, with α-(1→2) and α-(1→3) linked arabinose units (Dervilly-Pinel et al. 2004).

Efficient methods of physicochemical analysis and characterization of these polysaccharides are fundamental to understand their structure and their role in the plant source. The structure/characteristic of the hemicellulose can be the key for an appropriate application. In this chapter, topics related to chemical, physicochemical, and biological properties of hemicellulose and its derivatives were presented.

### 5.1.1 Composition of Hemicelluloses

Hemicelluloses are the second most abundant renewable polysaccharide on the planet, second only to cellulose (Sun et al. 2001; Peng et al. 2009). They are classified as heterogeneous polysaccharides, found in large quantities in wood and perennial plants, forming, together with cellulose and lignin, the plant cell wall (Peng et al. 2009). However, hemicelluloses are strongly associated with celluloses via physical connections (Fig. 5.1) and hydrogen bonds, while they are joined to lignin by covalent bonds, which is characterized by the sharing of one or more electron pairs between atoms, being them mainly R (radical)-benzyl and ether bonds (Freudenberg 1965; Peng et al. 2009).

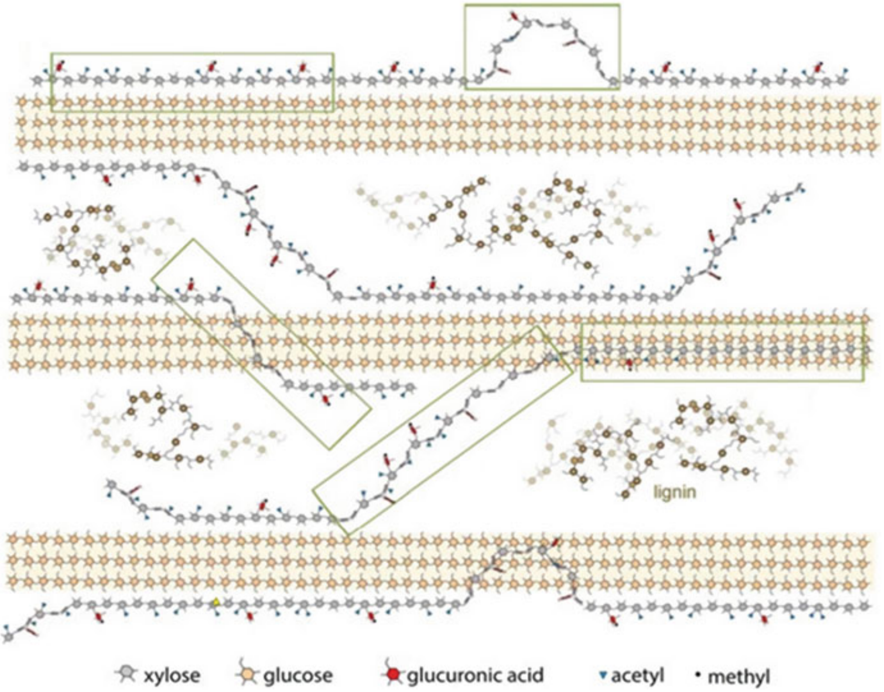


**Fig. 5.1** Scheme shows the complex structural organization between cellulose, hemicellulose, and lignin. This complexity is closely linked to the difficulty of separating hemicellulose between lignin and cellulose (Busse-Wicher et al. 2016)

In general, hemicelluloses are polysaccharides consisting of about 80–200 units of low molecular weight sugar residues. The general chemical formula of hemicelluloses is $(C_5H_8O_4)_n$, and is classified between pentoses and hexoses (Cai and Paszner 1988). Among the pentoses, the following stand out D-xylose, L-arabinose, and L-rhamnose; while among the hexoses the following sugars are more common: D-glucose, D-mannose, and D-galactose.

Hemicelluloses can also contain uronic acids, the most important being 4-*O*-methyl-D-glucuronic and D-galacturonic (Timell 1964). The most abundant hemicellulose in annual plants is arabinoxylan, which contains D-xylopyranosyl connected by β-(1-4) glycosidic bonds. Hemicellulose from sugarcane bagasse is defined as L-arabino-(4-*O*-methyl-D-glucurone)-D-xylan (Felipuci et al. 2021; Brienzo et al. 2009; Sun et al. 2004). Linked to them, as chains of simple units, in the positions C-2, C-3, or both, are residues of α-L-arabinofuranosis and α-D-glucuronic acid (or its 4-*O*-methyl derivative) (MacGregor 1993; Peng et al. 2009). Xylan, which is naturally occurring, contains *O*-acetyl groups located in some of the hydroxyl groups, in carbons 2 or 3, in its main chain (Peng et al. 2009).

Unlike cellulose, hemicellulose is not chemically homogeneous and its composition presents a great variation in proportion and content, depending on the species (Table 5.1), type of tissue, growth stage, and environmental and physiological

**Table 5.1** Amount of hemicelluloses from different biomasses

| Biomass | Hemicellulose (%) | References |
|---|---|---|
| Alfalfa stalks | 6.5 | Chandel et al. (2007) |
| Bamboo | 15–26 | Sánchez (2009) |
| Banana waste | 14.8 | Medina et al. (2006) |
| Banana waste | 14.8 | Sánchez (2009) |
| Barley straw | 27–38 | Saini et al. (2015) |
| Bast fiber Jute | 18–21 | Sánchez (2009) |
| Bast fiber Kenaf | 22–23 | Sánchez (2009) |
| Bast fiber Seed flax | 25 | Sánchez (2009) |
| Beet pulp | 36 | Zheng et al. (2013) |
| Bermuda grass | 35.7 | Prasad et al. (2007) |
| Coconut husk | 12 | Goh et al. (2010) |
| Coffee husk | 7 | Gouveia et al. (2009) |
| Coffee pulp | 46.3 | Sánchez (2009) |
| Coir | 0.15–0.25 | Saini et al. (2015) |
| Corn cob | 35–39 | Prasad et al. (2007), Kuhad and Singh (1993) |
| Corn fiber | 16.8 | Mosier et al. (2005) |
| Corn stover | 24–26 | Saini et al. (2015), Zhu et al. (2005) |
| Cottonseed hairs | 5–20 | Prasad et al. (2007) |
| Elephant grass | 24 | Sánchez (2009) |
| Food waste | 7.2 | Schmitt-Harsh et al. (2012) |
| General MSW | 9–16 | Li et al. (2012), Saxena et al. (2009) |
| Grass Esparto | 27–32 | Sánchez (2009) |
| Grasses (general) | 25–50 | Saini et al. (2015) |
| Hardwood | 45–50 | McKendry (2002) |
| Hardwood bark | 20–38 | Saini et al. (2015) |
| Hardwood stem | 24–40 | Sánchez (2009) |
| High–grade paper | 8.4 | Schmitt-Harsh et al. (2012) |
| Kraft paper | 9.9 | Schmitt-Harsh et al. (2012) |
| Leaf Fiber Abaca (Manila) | 17.3 | Sánchez (2009) |
| Leaf Fiber Henequen | 4–8 | Sánchez (2009) |
| Leaf Fiber Sisal (agave) | 21–24 | Sánchez (2009) |
| Leaves and grass | 10.5 | Schmitt-Harsh et al. (2012) |
| Miscanthus | 18–24.3 | Brosse et al. (2010) |
| Mixed or low-grade paper | 9.4 | Schmitt-Harsh et al. (2012) |
| Napier grass | 20 | Saxena et al. (2009) |
| Newspaper | 25–40 | Howard et al. (2003) |
| Nutshells | 25–30 | Howard et al. (2003) |
| Oat straw | 27–38 | Sánchez (2009) |
| Office paper | 12.4 | Mosier et al. (2005) |
| Orchard grass | 40 | Sánchez (2009) |

(continued)

**Table 5.1** (continued)

| Biomass | Hemicellulose (%) | References |
|---|---|---|
| Pine | 8.8–26 | Mosier et al. (2005), Olsson and Hahn-Hägerdal (1996) |
| Pineapple leaf fiber | 18 | Reddy and Yang (2005) |
| Poplar | 27.4–28.7 | Mosier et al. (2005), Olsson and Hahn-Hägerdal (1996) |
| Primary wastewater solids | 0 | Sánchez (2009) |
| Rice husk | 18–21 | Ludueña et al. (2011) |
| Rice straw | 23–28 | Saini et al. (2015) |
| Rye straw | 27–30 | Sánchez (2009) |
| S32 ryegrass (early leaf) | 15.8–25.7 | Sánchez (2009) |
| Silver grass | 25–35 | Sun and Cheng (2002) |
| Softwood | 35–40 | McKendry (2002) |
| Softwood bark | 15–33 | Saini et al. (2015) |
| Softwood stem | 25–35 | Sánchez (2009) |
| Solid cattle manure | 1.4–1.33 | Sánchez (2009) |
| Sorted refuse | 20 | Prasad et al. (2007) |
| Sponge gourd fibers | 17.4 | Guimarães (2009) |
| Sugarcane bagasse | 19–25 | Saini et al. (2015), Kim and Day (2011) |
| Sugarcane bagasse | 25 | Alves et al. (2020) |
| Sugarcane bagasse | 28.5 | Fernandes et al. (2020) |
| Sugarcane whole | 17 | Saxena et al. (2009) |
| Sweet sorghum bagasse | 18–27 | Saini et al. (2015) |
| Swine waste | 28 | Sun and Tomkinson (2002) |
| Switchgrass | 30–50 | McKendry (2002) |
| Waste papers from chemical pulps | 10–20 | Prasad et al. (2007) |
| Water hyacinth | 48.7–49.2 | Kumar et al. (2016), Nigam (2002) |
| Wheat straw | 26–32 | Saini et al. (2015) |

conditions (Martins et al. 2021; Melati et al. 2021; Fengel and Wegener 1984; Brienzo et al. 2010, 2014). There is a great variety in the content and composition of hemicellulose in the stems, leaves, roots, and bark. For example, wheat hemicellulose has different degrees of substitution between tissues. The arabinose/xylose ratio is equal to 1, when analyzing the outer part of the grain (pericarp), while the inner part has a low degree of substitution (0.3) (Brillouet and Joseleau 1987). Xylan is the main polysaccharide found in hardwood hemicelluloses, while mannan is prevalent in softwoods (Gao et al. 2013). Hemicellulose has an amorphous and hydrophilic structure, therefore, it is easier to remove from cell walls than cellulose. Xylose and xylooligosaccharides are often the main products obtained from pretreatment and enzymatic hydrolysis of hemicellulose (Forsan et al. 2021), and can be used as fermentable sugars for ethanol generation, for example (Gao et al. 2013).

Other value-added products or intermediate compounds, such as xylitol, furfural, and levulinic acid, used for the production of chemicals and polymers, also can be generated from hemicellulose through appropriate catalytic approaches (Aden et al. 2004; Alonso et al. 2010). Other authors have suggested that content, as well as hemicellulose composition, can also affect cell wall recalcitrance (York and O'Neill 2008). Interactions between hemicellulose microfibers and cellulose, as well as lignin-carbohydrate bonds, are able to prevent the enzymes attack (Chundawat et al. 2011; Hsu 1996). Transgenic *Arabidopsis*, with lower content of methyl groups in the glucuronoxylan side chains, released more xylose than the wild-type control in less severe conditions after enzymatic hydrolysis (Urbanowicz et al. 2012).

In view of all these hemicelluloses characteristics, some mechanisms help in the characterization of these materials. For this purpose, some methods aim to find the compositions of these materials, both physical and chemical, as well as to identify their chemical structure. Some of these methods are described in the following topics.

## 5.2 Physical-Chemical Analytical Methods of Hemicelluloses

### 5.2.1 Chemical Characterization

The methodology used to determine the chemical composition of biomass is extremely important in studies of lignocellulosic materials valorization. In particular, the development of processes for the production of ethanol from sugarcane biomass involves the optimization, in an integrated manner, of several stages: pretreatment, hydrolysis, and hydrolysates fermentation. To evaluate the efficiency of different alternative processes, an accurate biomass chemical characterization during its conversion in the different stages involved is essential. For lignocellulose chemical characterization, acid hydrolysis with sulfuric acid is generally used. Thus, polysaccharide depolymerization occurs, forming oligomers and their constituent sugars, that is, their repetitive units. In the case of hemicellulose from grasses such as sugarcane bagasse and sorghum, the largest fractions are xylose, arabinose, and acetic acid (Martins et al. 2021; Alves et al. 2020; Gouveia et al. 2009).

### 5.2.2 High-Performance Liquid Chromatography (HPLC)

Several analytical techniques are applied for hemicellulose and high-performance liquid chromatography (HPLC) associated with different detection systems is one of them. For several advantages such as high resolution, fast analysis, direct injection of the sample without or with little pretreatment, and ease of automation, it is widely used. Many modes of operation of the HPLC are used in the analysis of sugars, such as those found in hemicelluloses (Fig. 5.2). Carbohydrate HPLC is performed regularly using cation exchange resins based on copolymers in protonated or metal ion forms. Strong cation exchangers with metallic charges, such as sulfonated

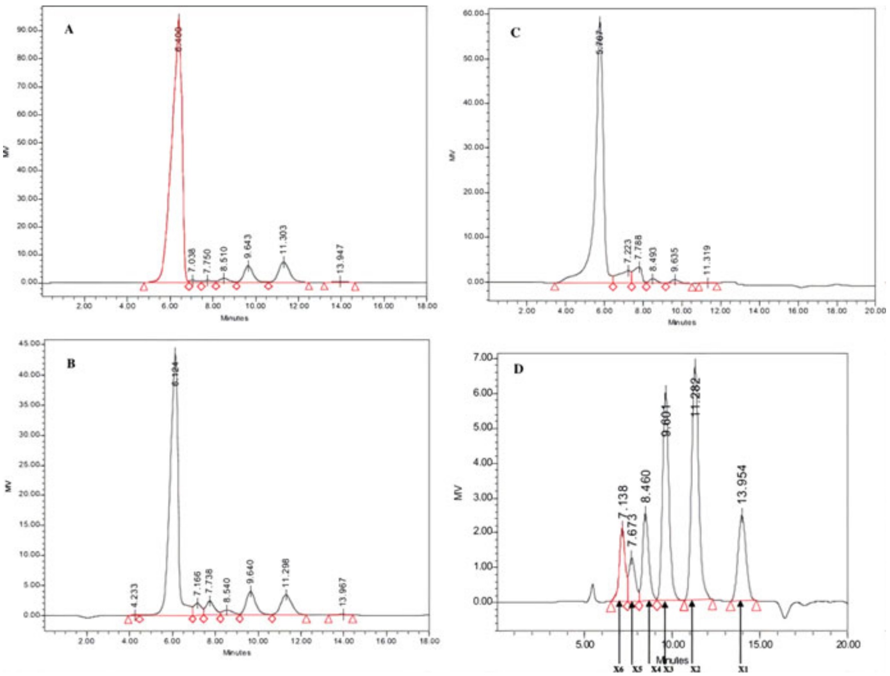


**Fig. 5.2** Example of HPLC profiles of soluble xylan degraded by immobilized rePBaxA. Note: (**a**–**c**) HPLC analysis of hydrolysates from beechwood, birchwood, and oat spelt xylan by rePBAxA at 40 °C for 6 h, respectively. (**d**) Standard xylooligosaccharide mixture analyzed by HPLC. The positions of xylose (X1), xylobiose (X2), xylotriose (X3), xylotetraose (X4), xylopentaose (X5), and xylohexaose (X6) are shown. The peak area of chromatographic parameter was used to quantify the xylooligosaccharides (Liu et al. 2017)

styrene-divinylbenzene copolymers in the form of calcium, lithium, sodium, lead, and silver, are often used in many mono and oligosaccharide separations. The charge of sulfonated resins with various cations is closely associated with substantial changes in the retention and selectivity of neutral carbohydrates. Thus, through the approaches, separations involving different mechanisms, such as ion exchange, ion exclusion, exclusion by size, ligand, and counter ion exchange, can be performed. Often, in these techniques, the subdivided sugars are chromatographed using pure water as the mobile phase (Huber and Bonn 1995; Fedorowski and LaCourse 2010).

Chromatographic systems of hydrophilic interaction using silica columns based on bound phase packaging and employing mixtures of acetonitrile-water as the mobile phase, as well as reverse phase chromatography, are also used for the separation of carbohydrates. However, these HPLC methods can suffer from several disadvantages, such as instability, the short service life of the connected phases, and poor column performance in selectivity and efficiency. In addition, the sensitive detection of carbohydrates after separation by HPLC represents an additional difficulty for their determination. In fact, carbohydrates mostly lack chromophores and fluorophores. This usually results in attempts to detect carbohydrates using low-wavelength UV absorbance or refractive index (IR) detection. It is known that neutral carbohydrates adsorb light only in the region of 190–210 nm, where organic modifiers of the mobile phase, such as acetonitrile, also strongly adsorb. Consequently, UV detection is unsuitable for use in HPLC of solubilized carbohydrates when mobile phases rich in these solvents are used. Greater detection sensitivity can be achieved by derivatization, introducing a chromophoric or fluorescent group in the carbohydrate analyte (Lamari et al. 2003).

Chemical derivatizations often cause an increase in detection selectivity, since only reducing sugars can change in the presence of amino acids and lipids when the carbonyl groups are derived. Non-direct UV absorption or indirect fluorescence detection has also been proposed. The detection of the refractive index (IR), after absorbance and fluorescence, is the third most important method in conventional HPLC and has been the most used in liquid chromatographic analysis of sugars. However, sensitivity to changes in the composition of the mobile phase has been the main disadvantage of detecting IR, preventing it from being used when gradient elution is chosen to be used. Consequently, the lack of selectivity and sensitivity of these detection methods, makes them, generally, insufficient for the analysis of carbohydrates present in complex mixtures, such as hemicelluloses. Alternatively, the detection of evaporative light scattering (ELSD) has also been proposed. ELSD is not sensitive to temperature fluctuations, in addition, it allows solvent gradient systems and depends on the mass of the vaporized analyte. However, ELSD requires vaporization of all components of the HPLC eluent and there must be no vaporization of carbohydrates so that they can be detected. Therefore, any gradient of eluents that require the lowest possible temperature can be used to avoid thermal degradation of carbohydrates. Consequently, the composition of the chromatographic mobile phase is not independent of the detection system. In conclusion, the detection by ELSD, considered a universal detector, presented almost no application in the analysis of carbohydrates by HPLC (Corradini et al. 2012).

Seven different mechanisms govern separations in HPLC. By changing the column and moving phase, it is possible to use each one in the same equipment. Next, some general notions about the mechanisms of HPLC and the classes of compounds that separate them will be mentioned.

#### 5.2.2.1 Liquid-Solid or Adsorption Chromatography

The separation mechanism in liquid-solid chromatography (LSC), or by adsorption, is based on the competition that exists between the molecules in the sample and those in the mobile phase in occupying the active sites on the surface of a solid (stationary) phase. For the solute molecule to be adsorbed on the stationary phase, a molecule from the mobile phase must first be displaced from the surface. Assuming that the adsorbent has a polar surface (for example, silica or alumina), support groups (for example, hydrocarbons) will have little affinity with this surface and, therefore, will not be retained.

Polar functional groups, capable of forming hydrogen bonds, will have strong surface affinities and will be strongly retained. Polarizable molecules (for example, aromatic molecules) will present dipole–dipole interaction with the adsorbent surface and, therefore, will also be retained. The degree of retention depends on the polarization of each molecule or functional group.

The stationary phase particles must have a large surface area, that is, a large number of active sites. The surface activity of many solids (including silica and alumina) is often affected by the retention of high-polarity molecules such as alcohols, phenols, water, etc. Due to them, on certain occasions, it is difficult to reproduce the results obtained in the analyzes, because the surface properties have suffered changes. As a result, the silica surface used in the HPLC is subjected to certain deactivation processes to reduce the retention of very polar molecules, thus, maintaining the surface in uniform conditions, which contributes to the improvement in the analyzes reproducibility (Corradini et al. 2012).

#### 5.2.2.2 Liquid-Liquid or Partition Chromatography

The separation mechanism in liquid-liquid chromatography (LLC) is based on the different solubilities that the sample components present in the mobile phase and the liquid stationary phase. The most soluble components in the stationary phase are selectively retained by it, while the least soluble components are transported more quickly by the mobile phase. LLC is used for slightly polar compounds, whose molar masses are less than 2000.

The drawback of this technique is the solubility of the stationary phase in the mobile phase, which quickly deteriorates the column, leading to non-reproducibility in the separations. This can be resolved in two ways. The first is to saturate the mobile phase with the stationary phase via a pre-column, placed before the injector, which contains a high percentage of the stationary phase. The second way is using materials that contain the stationary phase chemically bonded to a solid support, a technique to be described in the next section (Bottoli et al. 2004).

#### 5.2.2.3 Liquid Chromatography with Chemically Bound Phase

The stationary phase for chemically bound liquid chromatography (CBLC) arose as a consequence of the problems associated with LLC. Since the stationary phase is chemically bonded to the surface of a support, the problem of the solubility of the stationary phase in the mobile phase is eliminated. The main mechanism of this technique is based on the partition, leading some authors to consider it a liquid-liquid chromatography. On the other hand, this stationary phase also influences active (polar) groups on the support surface, which means that the adsorption mechanism also occurs, and because of that most researchers consider this technique to be different from the others (Bottoli et al. 2004).

By varying the nature of the stationary phase functional groups, it is possible to obtain different selectivities. Such groups may have a polar nature, such as the amino group (–NH), the nitrile group (–CN) or the diol group [$–CH_2(OH)_2$], which, functioning similarly to the polar phases of LSC, are called normal phase (FN). Groups can also be supportive in nature, such as the groups octyl ($–C_8H_{17}$), octadecyl ($–C_{18}H_{37}$), phenyl ($–C_6H_5$), etc., which represent the reverse phases (RP). The reverse phases, the so-called when the stationary phase is more supportive than the MP and occurs the reverse of the “normal” situation of classical liquid chromatography, are more commonly used in HPLC.

In normal phase chromatography, the less polar component of the sample is eluted first because it is not very miscible in the polar stationary phase. The medium polarity compounds then elute followed by the polar components, which interact strongly with the stationary phase. In reverse phase chromatography, retention will depend on the analyte hydrophobicity. The most polar compounds in the sample are weakly retained and eluted first, while the compounds supporting are most strongly retained.

### 5.2.2.4 Ion-Exchange Chromatography

In ion-exchange chromatography (IEC), the stationary phase is normally a resin of polystyrene intercrossed with divinylbenzene or based on silica, to which ionic groups such as the $SO_3$-group, in the case of the cation exchanger, or the NR3+ group, in the case of the anion exchanger, are attached. These ionic groups have a counter ion (with opposite charge) that can be displaced by the ions dissolved in the mobile phase. The mobile phase contains ions and ionic samples that compete with counterions to bind to the stationary phase through an ion-exchange mechanism shown below:

$$\mathrm{X} + +\mathrm{Marix} - \mathrm{R}\ \mathrm{Na}+ = \mathrm{Matrix} - \mathrm{R} - \mathrm{X} + +\mathrm{Na} + \text{(cationic exchanger)}$$

$$\mathrm{X} - +\mathrm{Matrix} - \mathrm{R} + \mathrm{Cl}- = \mathrm{Matrix} - \mathrm{R} + \mathrm{X} - +\mathrm{Cl} - \text{(anionic exchanger)}$$

Characteristic examples of compounds separated by IEC are carboxylic acids, sugars, analgesics, vitamins, inorganic anions, and metallic or complex cations. However, this technique can also be applied in the separation of peptides, amino acids, and nucleic acids, which can be ionized in solutions with properly buffered pH (Bottoli et al. 2004).

### 5.2.2.5 Bio-affinity Chromatography

In bio-affinity chromatography (BC), the separations occur due to highly specific biochemical interactions. The stationary phase contains specific groups of molecules that can only adsorb the sample if certain steric and/or charge-related conditions are satisfied, for example, the interaction between antigens and antibodies. Bio-affinity chromatography can be applied to isolate proteins, lipids, etc., from complex mixtures, without involving large expenses (Bottoli et al. 2004).

### 5.2.2.6 Chiral Chromatography

Chiral chromatography (CQ) is used to separate enantiomers, which are isomers whose mirror images are not overlapping. Enantiomers have a chiral center, a chiral carbon atom, an asymmetric center, or an asymmetric carbon. Enantiomers have the same chemical and physical properties, except the deviation of polarized plane light. Therefore, to separate the enantiomers, a chiral environment capable of recognizing and differentiating the two molecules is necessary.

The classic way of separating enantiomers by chromatography is the derivation of enantiomeric mixtures to form diastereoisomeric mixtures, which can be separated using a chiral stationary phase. Although in this case conventional phases can be used, the formation of the diastereoisomeric mixture is not always easy, making this process laborious.

The most attractive methodology is the direct separation with the use of chiral stationary phases. Direct resolution of enantiomers is possible as long as there is chiral recognition between the racemic mixture and the chiral selector. These chiral stationary phases are prepared from chiral molecules or polymers, adsorbed or chemically bonded to a support, usually silica (Bottoli et al. 2004).

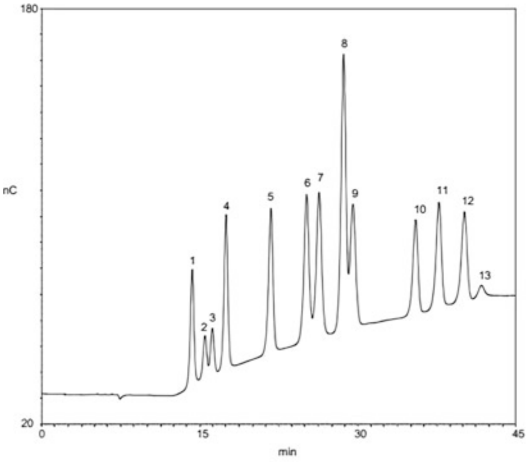
#### 5.2.2.7 Exclusion Chromatography

Exclusion chromatography (EC) separates according to the effective molecule size in relation to the pore size of the stationary phase. Small molecules can penetrate most pores and have a longer retention time, while larger ones are excluded from all pores and elute first. The range of molar masses that can be worked on by EC varies from approximately 1000 to several million. Classical EC employs fragile materials, unable to withstand pressures greater than 0.4 MPa. In contrast, HPLC requires materials with more rigid structures, such as silica or highly interlocking polymeric resins. Even though the literature contains examples of EC applications for the separation of organic and inorganic molecules with masses $<1000$, in aqueous and non-aqueous systems, the technique is predominantly used for the analysis of high molar mass compounds, including organic polymers (e.g., polyolefins, polystyrene, polyamides), silicones and biopolymers (e.g., proteins, nucleic acids, oligosaccharides, peptides, sugars, and glycols). The application of EC in polymers characterization has increased due to the determination of its molar masses distribution (Bottoli et al. 2004).

### 5.2.3 High-Performance Anion Exchange Chromatography (HPAEC)

High-performance anion exchange chromatography (HPAEC) is a great analytical tool for the separation of sugars due to its great ability to separate all classes of amino acids, alditols, mono, oligo, and polysaccharides, taking into account structural characteristics such as composition, size, anomericity, and binding isomerism. Also, the detector's insensitivity is overcome by the HPAEC coupling with pulsed amperometric detection. HPAEC-PED is currently being applied to a wide range of everyday research and monitoring applications. Besides, this technique greatly impacts the analysis of oligosaccharides and polysaccharides. The compatibility of electrochemical detection with the elution gradient, together with the high selectivity of the anionic exchange stationary phases, allow mixtures of mono, oligo, and polysaccharides to be separated with consistent resolution in a single run.

High-performance anion exchange chromatography is not widely used in the analysis of neutral carbohydrates. However, several carbohydrates are weak acids,



| **Peaks**: | (nmoles injected) |
|---|---|
| 1. Fuctiol | 10.0 |
| 2. GalNAcol | 2.0 |
| 3. GlcNAcol | unknown |
| 4. Xylitol | 10.0 |
| 5. Arabitol | 10.0 |
| 6. Sorbitol | 10.0 |
| 7. Dulcitol | 10.0 |
| 8. GlcNAc & GalNAc | 10.0 |
| 9. Mannitol | 10.0 |
| 10. Mannose | 10.0 |
| . Glucose | 10.0 |
| .2. Galactose | 10.0 |
| 13. Fructose | 50.0 |

Gradient Program

| Time (min) | %A | %B | Comment |
|---|---|---|---|
| -10.00 | 94 | 6 | Curve = 5 |
| 0.00 | 94 | 6 | Curve = 5 |
| 5.00 | 94 | 6 | Curve = 5 |
| 35.00 | 34 | 66 | Curve = 4 |
| 40.00 | 34 | 66 | Curve = 5 |
| 60.00 | 34 | 66 | Curve = 5 |

Note Equilibration Time:
10 min

**Fig. 5.3** Example of sugar separation chromatogram performed by Column CarboPac MA1 (Thermo Scientific 2013)

with p$K_a$ values in the range of 12–14 and, because of this, at high pH values, their hydroxyl groups are partially or totally transformed into oxyanions, which allows this class of compounds to be selectively eluted as anions by HPAEC in a single run. In alkaline media, sugars are separated with relative ease by quaternary anion exchange columns and linked to ammonium, where the order of increasing retention is closely related to the decreasing value of p$K_a$. Anion exchange chromatography on strong anion exchange columns based on high pH resistant polymers, specifically adapted for carbohydrate analysis, allows for the selective elution of these compounds, and the most important indices that influence separations are the number of hydroxyl groups, anomerism, positional isomerism, and the degree of polymerization.

The simplest sugars, such as monosaccharides, have several hydroxyl groups of great ionizable potential. Taking glucose as a reference, we arrive at the following acidity hierarchy: 1-OH $>$ 2-OH $\geq$ 6-OH $>$ 3-OH $>$ 4-O. Aldoses exhibit greater retention than their reduced forms of alditol. A study by Paskach et al. (1991), regarding the retention behavior of 93 alditols, the sugars in HPAEC demonstrated that, for monosaccharides, capacity factors are lower for alditols and are higher and approximately similar for aldoses and similar ketosis. Therefore, there is a general tendency, seen as stronger with alditols, of increasing the capacity factors associated with the increase in the number of carbon atoms.

The most common columns used in HPAEC-PED, designed specifically for anion exchange carbohydrate chromatography, are manufactured by Dionex (Sunnyvale, CA, USA; now Thermo Fisher Scientific Inc., USA). CarboPac MA1 (Fig. 5.3) is a fully functionalized macroporous resin with a strong and high capacity exchange column, while the others are prepared by proprietary processes, which allows the independent manufacture of sulfonated non-porous polymeric resins and exchange latex particles anionic functionalized with quaternary ammonium compounds that are collected only in the last stages of the preparation of the anion exchange columns (Corradini et al. 2012).

Monosaccharide separations are usually performed on CarboPac PA1 and CarboPac PA10 columns. This second has high selectivity for mono and disaccharide separations. Normally, these carbohydrates are isocratically eluted, using sodium hydroxide solutions in concentrations ranging from 10 to 20 mmol/L. In order to avoid the presence of carbon dioxide and the consequent production of carbonate in the mobile phase, the preparation of the eluents must pay special attention to carbonate as a divalent ion at pH 12. It binds strongly to anion exchangers and ends up causing interference with carbohydrate retention, reducing retention time, decreasing column selectivity, and loss of resolution. Efforts to solve this problem may depend on the use of an electrochemical generator of potassium hydroxide eluents that are not affected by carbonate interference. The use of barium and strontium ions in the alkaline eluent to reduce carbon dioxide uptake has been proposed (Cataldi et al. 1998). The separation of closely related sugars, such as glucose and mannose, which are different only in the axial/equatorial configuration of their hydroxyl groups, can be significantly increased by reducing the pH of the alkaline eluent to a value comparable to the $pK_a$ of the carbohydrate molecules, which is pH 12. Thus, in this case, the addition of a strong base via T-connection in the post-column elution current can generate the alkaline environment necessary for the detection of carbohydrates in the gold electrode of the detector.

The retention of oligosaccharides in the HPAEC column is not directly predictable beyond the hierarchy of hydroxyl acidity of monosaccharides in oligosaccharides. For members of the homologous oligosaccharide series, capacity factors are increased regularly and, even predictably, with chain length. However, in addition to the length of the chain, adding to the composition of the saccharides, it is expected that the binding positions affect the chromatographic retention of the oligosaccharides (Corradini et al. 2012).

CarboPac PA100 and CarboPac PA200, strong anion exchange columns, are regularly used for the characterization of oligosaccharides. A stronger eluent than sodium hydroxide is needed to elute oligosaccharides and polysaccharides up to DP 85. Sodium acetate solutions are normally used for those separations that still require sodium hydroxide since in a strongly basic environment, it is necessary for detection. Most oligosaccharide separations are done by a gradient of sodium acetate with a constant concentration of sodium hydroxide. The effects of acetate and nitrate as “pressure agents” have also been investigated. Wong and Jane (1995) compared the separations of disaggregated amylopectin, managing to add acetate or nitrate as anions in the mobile phases. According to what they found, compared to the commonly used pressure agent, nitrate tends to offer greater reproducibility, accuracy, and lower limit of detection.

### 5.2.4 Infrared Spectroscopy

Mid-infrared (MIR) spectroscopy has been used since 1950 for sugar structure analysis. Besides starch, some sugars that hold the most interest for the industry are sucrose, glucose, fructose, and xylose. However, water, which is a strong IR absorber, was shown to mask characteristic vibrational bands of sugars, and the spectra are consequently difficult to interpret (Cadet et al. 1997).

Hemicelluloses are widely used in the production of sugars, alcohols, organic acids, amino acids, plastics, furfurol, thickeners, and other products. Hemicellulose, a term that combines a group of polysaccharides, is constructed mainly of xylose (β-ᴅ-xylopyranose) units, occurs in all woody species, grains, and other plants. Xylans of deciduous species are predominantly hemicellulose polysaccharides and can be isolated from various woody plants. However, they can differ substantially in the main chain degree of branching, the ratio of xylose and glucuronic acid units, the number of acetylated groups, and the degree of polymerization. These macromolecules contain a whole set of various functional groups that can be identified by their vibrational spectra. This provides a basis for IR spectroscopic analysis of these compounds structures. IR spectroscopy is widely used for functional analysis of various polysaccharides and their complexes and also to study methylation process, presence of various structural groups, and intermolecular interactions. Vibrational spectroscopy is used successfully to study complicated natural polysaccharide complexes, of which xylan, in particular, is one (Buslov et al. 2009).

Spectroscopy is the study of the interaction between electromagnetic radiation and matter. Electromagnetic radiation is composed of an electric field vector and a magnetic field vector, mutually orthogonal, which propagate in a given direction. Electromagnetic radiation has wave–particle duality. The wave nature manifests itself through the interference, dispersion, polarization, and coherence of electromagnetic radiation. The corpuscular nature is manifested through the Compton effect. Electromagnetic radiation interacts with matter in three distinct processes: absorption, emission, and scattering of radiation. Vibrational spectroscopy studies the transition from normal molecular vibrations and comprises two techniques: infrared absorption and Raman scattering (Nakanishi and Solomon 1977).

The molecules have normal vibrations, which is their defined vibrational movement. These vibrations can be of the connection stretch type, angular deformation, and torsion. The normal stretching vibration can be symmetric, antisymmetric, degenerate, in phase, out of phase, and pulsation or ring breathing. The normal vibration of angular deformation can be of the symmetrical type, “wagging,” “twisting,” “rocking,” degenerated, in the plane, outside the plane, ring deformation, and torsion (Saranwong et al. 2004). The normal vibration calculated mathematically, considering the normal coordinates, previously defined in terms of the internal coordinates, is called normal mode (Coleman 1993).

Simple molecules or macromolecules are made up of atoms and form a three-dimensional structure, with chemical bonding distances and angles, presenting a certain molecular symmetry. The molecular structure is responsible for the different molecular properties, and for this reason, its knowledge is of the utmost importance in chemistry.

A molecule containing $N$ atoms will have $3N - 6$ normal vibrations (the number 6 represents the sum of three translations and three rotations along the orthogonal $x$, $y$, and $z$ axes) if its structure is non-linear; and $3N - 5$ normal vibrations, if it is linear (in this case, rotation along the axis of the molecule is excluded). For example, the water molecule ($H_2O$), with three atoms and a non-linear structure, will present $3 \times 3 - 6 = 3$ normal vibrations. The carbon dioxide molecule ($CO_2$), with three atoms and a linear structure, will present $3 \times 3 - 5 = 4$ normal vibrations (Saranwong et al. 2004).

As might be expected, this does not mean that the infrared spectrum or the Raman spectrum will have exactly $3N - 6$ vibrational bands for the water molecule or $3N - 5$ vibrational bands for carbon dioxide. The number of vibrational bands to be observed in the infrared or Raman spectrum will depend on the activity of these normal vibrations in the respective techniques, which will take into consideration the molecular structure, and the symmetry (point group) to which the molecule belongs. For a specific point group, the normal vibration that presents a variation in the dipolar moment, during the vibration, will be active in the infrared and a vibrational band will be observed in the IR spectrum. If normal vibration shows a variation in molecular polarization (induced dipole), during normal vibration, it will be active in Raman scattering and a band or line will be observed in the Raman spectrum. In the case of a molecular structure containing a center of symmetry, normal vibrations active in the infrared will not be active in Raman and vice versa. This is the well-known rule of mutual exclusion in vibrational spectroscopy. For molecular structures that do not contain a center of symmetry, some normal vibrations may be active in Raman and infrared, while other vibrations may be active only in IR or only in Raman (Kawano 2004).

Using the concepts of symmetry and group theory, it is possible to determine the set of normal vibrations active in IR and Raman. The normal $3N - 6$ or $3N - 5$ vibrations rise to the fundamental vibrational bands, whose number of waves usually appear in the spectral region below 4000 $cm^{-1}$. Depending on symmetry, the set may present normal vibrations distinct from the same energy, known as normal degenerate vibrations and, in this case, only one band will be observed in the IR spectrum. In a small molecule of high symmetry, degeneration of order two or three may occur. In the case of $CO_2$, the normal vibration of angular deformation in the horizontal plane and the vertical plane are two normal degenerate vibrations. The occurrence of normal degenerate vibrations reduces the number of bands observed in the IR spectrum or Raman (Kawano 2004).

In a vibrational spectrum, besides the fundamental bands, other bands may appear, such as combinations by sum or difference and harmonic bands (multiples of a fundamental band). In the region of low frequencies ($<500$ $cm^{-1}$), torsion bands, network mode bands (due to the movements of one chain in relation to others), and bands due to the acoustic mode (crystal vibration) may appear. In addition, some bands may be deployed due to the existence of normal vibrations, fundamental in phase and out of phase of adjacent groups, in a chain or between two normal vibrations, fundamental in phase and out of phase of adjacent groups, in a chain or between two normal vibrations of nearby chains, inside a unit cell (Kawano 2004).

Infrared absorption spectroscopy can be divided into three distinct regions:

10–400 cm$^{-1}$ IR far or away (FIR)
400–4000 cm$^{-1}$ average IR (MIR)
4000–12,820 cm$^{-1}$ Near IR (NIR)

Spectroscopy in the far or far IR (FIR) is little used in polymer studies because in this spectral range the vibrational frequencies of network modes, torsion modes, stretches and angular deformations of heavy atoms appear.

Most IR studies refer to the middle region (MIR), where the fundamental vibrational frequencies are located, corresponding to the vibrational transitions between the fundamental vibrational energy level ($v = 0$) and the first excited vibrational level ($v = 1$). The 400–1800 cm$^{-1}$ region is known as the fingerprint region of the IR spectrum since it is in this region that most of the fundamental vibrational frequencies occur (Á$v = 1$).

The near IR (NIR) region is developing intensively because of its use in quality and process control in industrial applications. Vibrational absorptions in the NIR correspond to the vibrational transitions between the fundamental energy level and higher energy levels ($v = 2, 3, 4, \ldots$), and/or a combination of a fundamental with other harmonics. In general, normal vibrations involving light atoms (CHO, $n = 1$, 2 and 3 and XH, X = N, S or O), which have strong bands in the fundamental region, usually appear in the NIR spectrum. Naturally, the relative intensity of the higher-order harmonic band becomes weaker as the harmonic order increases. In this case, it is customary to increase the thickness of the sample to increase the relative intensity of the bands (Kawano 2004).

Spectroscopy in the NIR associated with the chemometric technique was implemented for use in a quantitative determination in quality control and industrial process control. In vibrational spectroscopy, it is customary to refer to the position of the band in the spectrum by normal frequency instead of the number of waves, represented by the symbol $v$, which would be correct. This exchange of terms is permitted in everyday language because both terms are proportional to the energy of normal vibration (Kawano 2004).

After the MIR spectroscopy, the following values were found for the number of waves, frequency, and the time of a cycle:

400 cm$^{-1}$ 1.2 × $10^{13}$ Hz 0.8 × $10^{13}$ s
4000 cm$^{-1}$ 1.2 × $10^{14}$ Hz 0.8 × $10^{14}$ s

The vibrational frequencies of a molecule depend on the nature of the movement, the mass of the atoms, the molecule geometry, the nature of the chemical bonds, and the chemical/physical environment.

The devices used to obtain the IR spectrum are of two types: Spectrophotometric dispersive and Fourier transform spectrometer (FTIR). The dispersive spectrophotometer uses a monochromator with diffraction grating (or NaCl, KBr, or CsI prism) to decompose the infrared radiation. It is a type of device already in disuse since it is slow, expensive, and depends on high precision mechanics to scan the spectrum. The FTIR spectrometer uses the Michelson interferometer as a working principle, being faster, more accurate, reproducible, and accessible. The FTIR spectrometer consists of a radiation source, an interferometer, sample compartment, and an infrared radiation detector. The elements of an FTIR spectrometer vary according to the infrared regions under study. The routine commercial devices operate, normally, in a single region (MIR), and their elements are appropriate and fixed, but some spectrometers applied to the research are versatile, making it possible to replace the elements according to the region of interest. Some spectrometers can operate in the three infrared regions (FIR, MIR, and NIR) (Kawano 2004).

The most used source of infrared radiation in the FIR region is that of mercury vapor while in the MIR region, it is the Globar (CSi) (water-cooled), nickel-chrome spiral or ceramic stick, both air-cooled; and in the NIR region is the tungsten lamp (water or air cooler). Michelson's interferometer consists of a beam splitter (beamsplitter), a fixed mirror, and a movable mirror (the displacement of this mirror can be mechanical or by an air cushion). The configuration of the interferometer varies greatly from the spectrometer to spectrometer, according to the manufacturer, with the beam divider varying according to the spectral region (Kawano 2004).

A Mylar film (poly(ethylene terephthalate)-PET-of different thicknesses) is used in the FIR, the KBr, and the $CaF_2$ or the quartz NIR in the MIR. The KBr beam splitter is formed by a pair of KBr windows separated by a layer of germanium coating, which offers the specific property of dividing the infrared beam into two equal parts, reflecting half and transmitting the other half. All beam splitters contain a small, semi-mirrored central disc, reserved for 632.8 nm radiation from the He-Ne laser, used for alignment and data acquisition control (Kawano 2004).

The spectrometer detector also varies according to the regions of the IR. Thus, in the FIR, the bolometer or DTGS-polyethylene (deuterated triglycine sulfate with polyethylene window) are used, in the MIR the DTGS (less sensitive and slower, with KBr window), MCT (Mercury cadmium telluride-HgCdTe, cooled to temperature liquid nitrogen, more sensitive and faster) or the photoacoustic, and in the NIR the Si, InSb or PbSe are used (Kawano 2004).

Typically, the spectrometer configuration operates in the continuous scan. In the 90s, the FTIR spectrometer configuration, called step-scan, was developed, where, in the first step, one mirror is fixed and the other undergoes small punctual oscillation (dithers); in the next step, the fixed mirror is moved to a multiple distances of the wavelength of the He-Ne laser radiation (632.8 nm) and the operation is repeated, and so on until the fixed mirror reaches a displacement compatible with the chosen experimental conditions. This spectrometer configuration is used for time-dependent studies and comprises the most advanced techniques in the area of infrared spectroscopy (Kawano 2004).

### 5.2.5 X-Ray Techniques

Regarding lignocellulosic materials, X-rays are often used as a non-destructive technique, while 2D scanning is often considered a “destructive” technique because it is commonly used for elements extracted from a matrix. Both 3D and 2D imaging techniques provide useful morphological descriptions of lignocellulosic compounds, especially in annual plant biomasses.

The absorption principle of X-rays consists of reconstructing the attenuation coefficient from measurements of an X-ray beam attenuation passing through the sample in different viewing angles. Differences in the linear attenuation coefficient between the fibers are responsible for the contrast of the X-ray image, which allows the creation of two-dimensional images of the object’s internal structure. The reconstructed consecutive slices provide a high-resolution 3D volume visualization, allowing morphological measurements of microstructure parameters, such as porosity, effective area, or fiber diameter in a thermoplastic composite (Hamdi et al. 2015). Knowledge of these characteristics may be essential to determine the quality of biotechnological materials from lignocellulosic raw material, with special emphasis on hemicelluloses. The analytical methods based on X-rays are as follows: X-ray absorption, X-ray fluorescence, and X-ray diffraction.

The X-ray absorption has the same general application as other electromagnetic radiation absorption techniques (such as infrared, ultraviolet, etc.), providing information about the material’s characteristics (such as concentration and sample thickness). The best applications of the technique occur when the element under analysis (preferably a “heavy” atom) is dispersed in a matrix consisting of atoms of low atomic weight (which will absorb little or no incident radiation). This allows, for example, the determination of catalyst residues in polymers. However, X-ray absorption has not been used for this purpose because another X-ray method (fluorescence) has a much higher analytical potential, providing qualitative and quantitative information, and using the same type of equipment. Certainly, the most usual application of X-ray absorption is found in medical diagnostic imaging (radiographs), where, by varying the intensity of the X-ray beam, images of both bones (absorb X-rays intensely) and other tissues can be obtained (Neto 2004).

The X-ray fluorescence is an excellent technique, mainly for determining chemical constitution in ceramic and metallic samples, but also polymers. An X-ray fluorescence spectrum allows the detection of the presence of atoms that participate in molecules of additives, catalysts, mineral charges, etc., allowing their qualitative and quantitative determination, as a routine analysis. For quantitative analysis, calibration curves must be prepared in advance. The detection limit can reach levels of parts per million (ppm) (Neto 2004).

X-ray diffraction is applied in macromolecules and polymers that can form crystals in the same way as inorganic compounds, minerals, etc., with whose crystalline structures we are most familiar with (such as sodium chloride, for example). This technique uses the coherent scattering of X radiation, through organized structures (crystals), allowing to perform morphological studies on materials, determining their crystalline structure and their crystalline fraction (percentage). There are alternative methods to determine the percentage of crystallinity, such as density and differential scanning calorimetry (DSC). The determination of the unit cell (the smallest component of a crystal), however, is only feasible by diffraction techniques (Neto 2004).

### 5.2.6 Nuclear Magnetic Resonance (NMR)

The effects of nuclear magnetic resonance (NMR) on the matter were first detected in 1945, independently, by Purcell, Torrey, and Pound at Harvard and by Block, Hansen, and Packard at Stanford. In 1952 Purcell and Bloch obtained the Nobel Prize in physics for their discoveries (Abraham 1978).

The use of NMR in polymers was started in the 60s, with proton NMR (’H). Interest increased in the 1970s, with the application of 13 (13C) carbon NMR along with Fourier transform technology. Recently, advanced techniques such as two-dimensional NMR and multinuclear NMR have been increasingly adopted, and solid-state NMR is being developed for the study of polymers.

There is little evidence about xylan conformation in plant cell walls, and any tools that could detect conformations of native polysaccharides within intact cell walls would prove invaluable for future investigations about cell wall architecture (Dupree et al. 2015). One reason for this scarcity of evidence is the practical limitations of testing molecular architecture hypotheses; the disruptive chemical and biochemical methods used to elucidate the composition of cell walls are not subject to such investigations. Solid-state NMR (ssNMR), however, has the potential to produce information about the native arrangement of cell wall components because this technique does not require potentially disruptive preparation. In addition, NMR is useful for probing the conformation of carbohydrates, since conformations $2_1$ and $3_1$ in linked glycans (1→4) exhibit characteristic changes in C4 resonances (Jarvis and Apperley 1995). Hong and colleagues pioneered the use of multidimensional ssNMR to probe the molecular architecture of *Arabidopsis* primary hypocotyl cell walls uniformly labeled with $^{13}$C (Dick-Perez et al. 2011; Wang et al. 2013). These and other authors show and suggest that only a small part of the main hemicellulose, xyloglucan, interacts with cellulose, challenging conventional models of the primary cell wall (Dick-Perez et al. 2011; Wang et al. 2013; Bootten et al. 2004). ssNMR studies of secondary cell walls have been less intensive: some have used one-dimensional ssNMR (1D) to analyze the secondary cell walls distinct from *Arabidopsis*, fir wood (Ha et al. 2002; Fernandes et al. 2011), and corn (Foston et al. 2012). However, the limited resolution provided by 1D ssNMR makes it difficult to distinguish the many peaks that share similar chemical changes. The best resolution of two-dimensional (2D) ssNMR was explored to study the industrially important secondary cell wall of poplar (Bardet et al. 1997; Lesage et al. 1999) and corn (Komatsu and Kikuchi 2013). However, complete ssNMR studies of *Arabidopsis* model plant native secondary cell wall are the most urgent, as these would contribute most to understanding the roles of the secondary cell wall biosynthetic machinery, as well as benefit from the large set of mutants synthesis of the

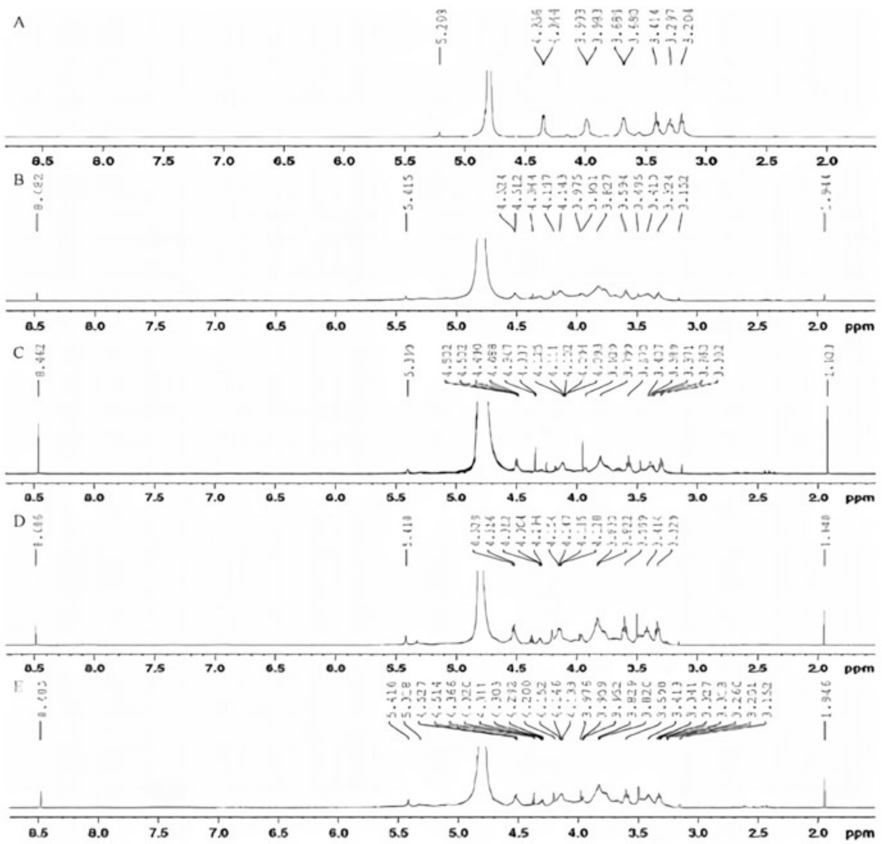


**Fig. 5.4** 1H NMR spectra of samples of xylan from sugarcane parts: (**a**) bagasse; (**b**) leaf; (**c**) external fraction; (**d**) internode; (**e**) node (Melati et al. 2021)

biochemically characterized *Arabidopsis* cell wall. Here, the first multidimensional ssNMR analyzes of *Arabidopsis* stems rich in the untreated secondary cell wall are reported. The *Arabidopsis* $^{13}$C labeled material was studied using a variety of $^{13}$C ssNMR methods, showing that the technique can probe the molecular environments of cellulose and xylan in the native secondary cell wall. The signals corresponding to a range of cell wall polymers, including xylan and the two characteristic domains of cellulose, were observed. Interestingly, the chemical changes in xylan differed significantly from those of the previous solution and the primary studies of the cell wall. This indicates that xylan is found in distinct conformations on the dry plant cell walls. It was also possible to identify intermolecular spatial connections between cellulose and other components of the cell wall (Dupree et al. 2015). An example of xylan NMR is shown in Fig. 5.4.

The NMR technique (theoretical fundamental princles- Cunliffe 1978) takes advantage of the property of some nuclei to present non-zero magnetic moments (and consequently spin). The quantum spin number, $I$, of atoms is related to their mass number, $A$, and atomic number, $Z$:

- If $A$ and $Z$ are even, $I = 0$.
- If $A$ is odd and $Z$ is odd or even, $1 = 1/2, 3/2, 5/2$, etc.
- If $A$ is even and $Z$ is odd, $/ = 1, 2, 3$, etc.

The most frequently studied nuclei on NMR are: 1H, 2H (D), 11B, 13C, 14N, 17O, 19F, and 31P.

The magnetic moment $p$ is related to nuclear spin by the following relation:

$$\mu = hy/2\pi$$

where $h$ = Planck constant and $y$ = giromagnetic constant.

If a nucleus is subjected to a strong magnetic field, its magnetic moment, $\mu$, tends to align with the field, which is accompanied by energetic changes. The nucleus is not completely parallel to the field but undergoes a precession movement.

## 5.3 Hemicellulose Bioactivity

As a renewable green resource, hemicelluloses can be widely used in the chemical, food, and paper industries. Moreover, it has been reported that they can also present several biological properties important for the medical field such as antioxidant, anticoagulant, and antimicrobial activities, as an inhibitor of cancer cell proliferation, among other biofunctions (Cantu-Jungles et al. 2017; Zhao et al. 2020). Antioxidants can significantly delay or prevent cell oxidative stress, which is known to cause the development and progression of several diseases, anticoagulants can prevent the formation of blood clots, suppressing the synthesis of molecules normally present in the blood. There are still limited therapeutic options to combat problematic infections and the resistance of microorganisms to several antibiotics makes the studies about new antimicrobial agents of fundamental importance (Mestechkina and Shcherbukhin 2010; Kasote et al. 2015; Lagadinou et al. 2020).

To determine antioxidant activity, the most common method used to evaluate the ability of compounds to scavenge free radicals is the model of stable radical 2,2-diphenyl-1-picrylhydrazyl (DPPH). The hydrogen-donating antioxidants are able to reduce the stable DPPH radical to a yellow-colored molecule (Von Gadow et al. 1997). Hemicellulose from almond gum presented concentration-dependent and antioxidant capacity when compared with butylated hydroxyanisole (BHA), a synthetic antioxidant. At the higher concentration used, 20 mg/mL, the antioxidant capacity of hemicellulose was 92.5% while BHA was 96.5% (Bouaziz et al. 2016). Scavenging activity of *Lentinus enodes* (cultured with hemicellulose) and *Caulerpa lentillifera* was also concentration-dependent, however, for the latter, at concentrations of 5, 10, and 20 mg/mL, the antioxidant activity has stabilized in an average of 78% scavenging activity (Liang et al. 2015; Wu et al. 2019).

ABTS (2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid)) radical is also widely used to evaluate the antioxidant activity of natural compounds by a decolorization assay (Re et al. 1999). Xylan from *Caulerpa lentillifera* presented a total antioxidant status equivalent of 166.9µg/mL trolox in a sample concentration of 5 mg/mL (Wu et al. 2019). Hemicelluloses from wood and rice rusk also showed antioxidant activity by this method. Rice rusk presented ABTS scavenging activity of 80% at the concentration of 5 mg/mL, while *E. globulus* wood and *P. pinaster* wood hemicellulose showed the same scavenging activity at a concentration of 10 mg/mL (Rivas et al. 2013).

Total antioxidant activity (TAC) of corn cob xylan was determined using phosphomolybdenum blue complex. In this test, the antioxidant compounds reduce $Mo^{6+}$ to $Mo^{5+}$ and there is the formation of green $Mo^{5+}$, which can be quantified by absorption at 695 nm. Corn cob presented TAC corresponding to 48.5 mg of ascorbic acid equivalent per g of xylan (Melo-Silveira et al. 2012). The reducing power capacity of almond gum hemicellulose was determined by the reduction of $Fe^{3+}$ to $Fe^{2+}$ and quantified by absorption at 700 nm, since the test solution yellow color changes to green or blue depending on the antioxidant capacity to donate electrons. At a concentration of 20 mg/mL, the reducing power of almond gum hemicellulose was similar to that of BHA (Bouaziz et al. 2016).

The interest in the use of polysaccharides for the synthesis of anticoagulants has been increasing due to their biocompatibility, biodegradability, and non-toxicity (Cheng et al. 2017). Anticoagulant polysaccharides exhibit this activity due to the presence of charges, primarily sulfate groups. Sulfated hemicelluloses from several sources showed anticoagulant activity, which can vary depending on structural specificities such as the sulfate group position (Melo-Silveira et al. 2012).

To evaluate anticoagulant activity from corncob xylan, activated partial thromboplastin time (aPTT) and prothrombin time (PT) assay were performed using commercial kits and clotting time (the time required for a blood sample to clot in vitro under standard conditions) was determined by an automatic coagulometric. To determine the influence of xylan anticoagulant in extrinsic coagulation, a PT test was performed and clotting time showed no increase in any of the conditions tested. However, when the intrinsic coagulation pathway was analyzed by aPPT test, it was observed that increasing the dosage of xylan, the clotting time was prolonged. At a dose of 100µg of xylan plasma, the clotting time was double when compared to the control (Melo-Silveira et al. 2012).

Another research also evaluating sulfated corncob xylan anticoagulant activity showed similar results. APTT was prolonged in a dose-dependent manner when compared to the blank control and the PT of sulfated xylan samples had no significant prolongation within concentrations used in the experiment (Cai et al. 2015). Sulfated xylan from sugarcane bagasse was also submitted to anticoagulant assays. The aPPT test showed that sulfated xylan effectively extended clotting time when compared to the blank in a dose-depending way and had a similar anticoagulant activity to heparin. Despite that, sugarcane bagasse sulfated xylan showed no significant effect on PT assay, regardless of the concentration used. These results,

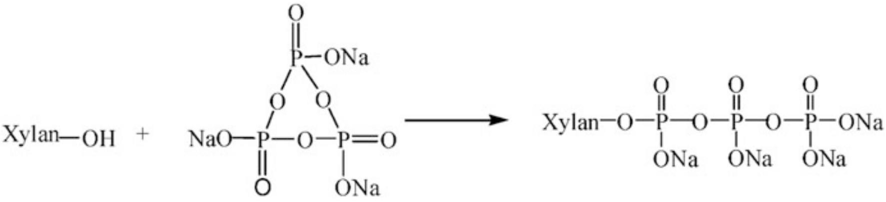


**Fig. 5.5** Phosphorylated birchwood xylan produced under alkali conditions using trisodium trimetaphosphate (STMP)

similar to other reported sulfated hemicellulose, suggest that they affect mainly the intrinsic coagulation pathway (Chen et al. 2020).

Besides sulfate groups, carboxyl groups of glucuronic acid residues present in the xylan structure may also be involved in the anticoagulant activity. Xylan from corncob was submitted to a carboxy-reduction process in order to evaluate the participation of carboxyl groups in the anticoagulant activity. After a reduction of 70% of carboxyl present in the corncob xylan, its anticoagulant activity presented a drastic decrease, indicating that these groups have an important part in the anticoagulant activity (Melo-Silveira et al. 2012).

Antimicrobial activity of phosphorylated hemicelluloses against *E. coli*, *Staph. Aureus,* and *C. albicans* was evaluated by the well diffusion method, using nutrient agar for bacteria and PDA for yeast. Samples containing palm frond and rice straw hemicelluloses were tested and were effective against all pathogens, however, in different degrees. Phosphorylated palm frond hemicellulose presented the highest antimicrobial activity, which can be related to its high antioxidant action, also evaluated in the same study (Pepeljnjak et al. 2005; Ragab et al. 2018) (Fig. 5.5).

Also using the agar diffusion method, the antimicrobial potential of almond gum hemicellulose was tested against bacteria pathogenic strains such as *Actinomycetes* sp., *Salmonella typhimurium*, *Klebsiella pneumonia*, *Listeria monocytogenes*, *Staphylococcus aureus*, *Salmonella enterica*, *Pseudomonas aeruginosa*, *Bacillus thuringiensis,* and *Bacillus subtilis*. Almond gum hemicellulose showed a strong antibacterial effect at 40 mg/mL against *B. thuringiensis*, *S. enterica,* and *P. aeruginosa* and moderate effect against *A.* sp., *S. typhimurium*, *K. pneumonia*, *L. monocytogenes,* and *B. subtilis* (Bouaziz et al. 2016).

A xylan-based antimicrobial additive for use in paper products was evaluated against *E. coli* by measuring the diameter of the inhibition zones. A commercial xylan extracted from sugarcane bagasse was submitted to a cationization process. The cationic-xylan was copolymerized with guanidine using ceric ammonium nitrate as an initiator. This molecule was added to the paper to improve mechanical properties and it also showed an efficient antimicrobial activity against *E. coli* (Xu et al. 2020).

Xylan from agave bagasse was functionalized with trimethoxysilylpropyl methacrylate (TMSPMA) and poly(*N*-vinylcaprolactam) in order to obtain a thermoresponsive hydrogel with potential for drug delivery applications. Ciprofloxacin, a model drug with great antibacterial efficacy for both gram-positive and gram-

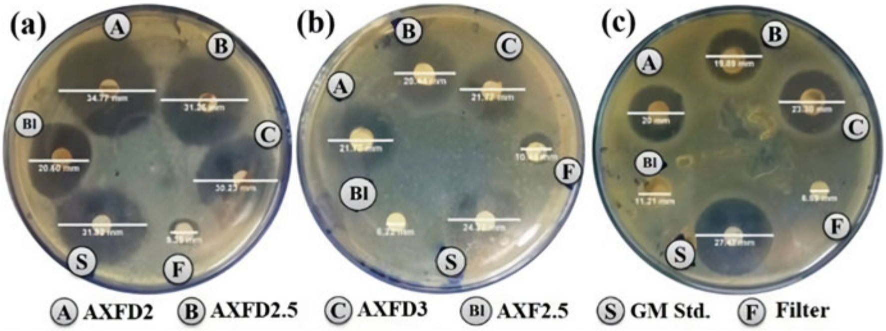


**Fig. 5.6** Antibacterial activity of films against (**a**) *S. aureus*, (**b**) *E. coli*, and (**c**) *P. aeruginosa*

negative bacteria was used to test the loading and releasing capacity of the hydrogel. The material showed a capacity to absorb ciprofloxacin in concentrations higher than the MIC and inhibited the growth of *E. coli*, *S. aureus,* and *P. aeruginosa*. Moreover, the hydrogel exhibited a releasing efficacy for 3 days at 37 °C, which is a desirable characteristic for a formulation that can be applied in surgical wounds (Arellano-Sandoval et al. 2020).

A film composed of 2–3% of arabinoxylan isolated from psyllium husk was submitted to an in vitro release study, using gentamicin as an antibiotic model, to determine antibacterial activity of the loaded films by disk diffusion test, measuring the zone of inhibition on the plates. The film containing 2.5% of arabinoxylan and 0.1% gentamicin (AXFD2.5) released approximately 45% of the antibiotic in the first hour and reached maximum release after 12 h, while the film containing 3% arabinoxylan and 0.1% gentamicin (AXFD3) release 25% of the antibiotic in 1 h and maximum release occurred only after 16 h. This indicates that the film with a higher content of arabinoxylan has a formulation that is more appropriate to deliver the antibiotic at the wound site since it can maintain a level of the drug for a longer time (Ahmad et al. 2020).

The blank arabinoxylan film presented no antibacterial activity against *E. coli* and *P. aeruginosa* (gram-negative bacteria) (Fig. 5.6). However, a significant effect was observed against *S. aureus* (gram-positive bacteria), which suggests that the pure arabinoxylan film has an antibacterial activity itself. All films loaded with gentamicin showed activity against all the bacteria tested. To ensure safety to use the film for wound-dressing, a cytocompatibility test was performed. The results revealed that more than 90% of cells, treated with samples of blank and antibiotic-loaded arabinoxylan films, were viable after 24 h and can be considered safe for further in vivo investigations (Ahmad et al. 2020).

Corn cob xylan presented an antiproliferative activity against tumor cells in a dose-dependent manner, reaching a maximum of 50% for a sample with a concentration of 2 mg/mL (Melo-Silveira et al. 2012). Almond gum hemicellulose showed to have promising potential to inhibit angiotensin-converting enzyme (ACE), which plays an important role in the regulation of blood pressure by raising it. The concentration of hemicellulose used to inhibit 50% of this enzyme activity was 0.73 and at 1 mg/mL, the inhibition reached 90% (Bouaziz et al. 2016).

Oligosaccharides from hemicellulose, such as xylooligosaccharides (XOS), can also present biological properties. Due to the presence of phenolic content in different organic waste materials, XOS can present good antioxidant activity (Rashad et al. 2016). XOS produced by enzymatic hydrolysis of beechwood and birchwood glucuronoxylans were tested to evaluate their antioxidant activity, which was measured by the quantification of ABTS radical discoloration. The antioxidant activity of XOS from beechwood xylan was around 80% at a concentration of 200 μg/mL xylose reducing equivalent, while the result of XOS from birchwood xylan was higher, a 100% antioxidant activity at 150 μg/mL xylose reducing equivalent. Moreover, XOS degree of polymerization affected the antioxidant activity, showing an increase of activity along with the increase of degree of polymerization (Valls et al. 2018).

To evaluate its antioxidant activity, XOS from *Moso* bamboo were analyzed in radical-scavenging assays using DPPH and hydroxyl radicals and showed a dose-depending activity. At a concentration of 2.5 g/L, the scavenging activity was 85.7% and 65.5% for DPPH and hydroxyl radical, respectively. IC50 (antioxidant concentration required to quench 50% of the initial radical) of XOS for DPPH and hydroxyl radicals was 1.1 g/L and 1.7 g/L, respectively (Huang et al. 2019). The antioxidant activity of XOS from sugarcane bagasse was also concentration-dependent. Scavenging activity for DPPH at 0.1, 0.2, 0.4, 0.6, and 0.8 mg/mL were 20.1%, 27.3%, 36.1%, 48.6%, and 62.1%, respectively, and increased gradually until reaching 84.5% at a concentration of 2 mg/mL (Bian et al. 2013).

Other positive effects of XOS are related to the optimization of probiotics metabolism. Beneficial bacterial can produce XOS degrading enzymes to ferment them and produce short-chain fatty acids (SCFA) such as acetate, propionate, and butyrate, which will help in the acidification of the bowel and provide metabolic energy for the host (Patel and Prajapati 2015). The role of prebiotics such as XOS for enhancing immune status is being studied. The addition of 0.05% XOS to feed improved the immune function in laying hens by positively influencing the gut microbiota and production of short-chain fatty acids. The growth performance in fish and poultry was also affected by the addition of XOS to feed (Samanta et al. 2015; Huang et al. 2019).

Xylooligosaccharides from rice husk presented an antihyperglycemic effect in the type 2 diabetic rat model. Supplementation with XOS for 12 weeks decreased the plasma glucose and insulin levels and increased SCFAs production, achieving good glycemic control by the maintenance of gut microbiota (Khat-udomkiri et al. 2020). XOS are also being studied for the suppression of carcinoma cells, mainly breast and colon cancer, and potential for synthesizing vitamins due to their activity on *Bifidobacterium* (Akhtar and Swamy 2018).

## 5.4 Concluding Remarks

Hemicelluloses are extremely important polysaccharides, especially if evaluate the great biotechnological potential that it presents. However, there is a long way to go through pretreatment or treatment before it can be used for these purposes. And for that, there is a need to increasingly improve the ways of obtaining and characterizing this material, chemical, physical and/or biologically. As shown in this chapter, several viable and important mechanisms (between techniques and equipment) can give valuable information about the chemical composition, physical, morphological and spatial structure of these polysaccharides. It is fundamentals to seek continuous improvement of these techniques and also to share new information about it, since, as shown, there is no unanimity on the best ways to carry out the physical-chemical and biological characterizations of hemicelluloses. Therefore, more research must be done to improve, cheapen, and optimize the processes of characterization and analysis of these compounds. Fast, cheap, and accurate methods of polysaccharides characterization can contribute to the industrial large-scale. The quality of the production of biotechnological derivatives is fundamentals to obtain products with higher yield and quality since the bioproperties of a hemicellulose will depend on its characteristics.

**Acknowledgments** The authors thank the São Paulo Research Foundation (FAPESP grant number 2017/22401-8; 2019/12997-6) for financial support.

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# 6

# Chemical Modification Strategies for Developing Functionalized Hemicellulose: Advanced Applications of Modified Hemicellulose

Júlia Ribeiro Martins, Mateus Manabu Abe, and Michel Brienzo

## Abstract

Hemicellulose is a highly hydrophilic homo or heteropolysaccharide with a branched structure. This polysaccharide exhibits great potential as a feedstock material, and a derivatization results in the formation of better feedstock material. Hemicellulose can be used as a bio-polymeric material as it is biodegradable. It also exhibits the advantage of being renewable and it is available in residues/waste. The backbone of the hemicelluloses and the side chains contain a large number of hydroxyl groups. Esterification, etherification, graft copolymerization, and other reactions can be conducted to chemically modify these hydroxyl groups. The chemical modifications help tune various properties such as hydrophobicity, thermal stability, and solubility (in different solvents). The free hydroxyl groups present in the macromolecules can be chemically modified to other functional groups to address the drawbacks. The modified compounds can find applications in various fields and their novel properties can be exploited.

## Keywords

Esterification · Etherification · Bioplastic · Hydrophobicity · Thermal stability · Solubility

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M. Brienzo (ed.), *Hemicellulose Biorefinery: A Sustainable Solution for Value Addition to Bio-Based Products and Bioenergy*, Clean Energy Production Technologies, https://doi.org/10.1007/978-981-16-3682-0_6

## 6.1 Introduction

Hemicellulose is a renewable and widely available polysaccharide associated with cellulose present in lignocellulosic biomass. It accounts for approximately 20–35% of plant biomass such as corn stalk (30.3%) (Dong et al. 2018), empty fruit bunch (26.64%) (Zawawi et al. 2018), meadow grass (28.14%) (Tsapekos et al. 2018), sorghum straw (32.57%) (Hernández-Beltrán and Hernández-Escoto 2018), sugarcane bagasse (23.27%) (Fernandes et al. 2020), elephant grass (23.93%) (Santos et al. 2018), spent coffee ground (28.12%) (Chiyanzy et al. 2014), and wheat straw (26.9%) (Shah and Ullah 2019). The hemicelluloses in their natural states are amorphous and branched polymers of low molecular weight. The structural characteristics of the hemicelluloses can be attributed to the heterogeneous chemical constituents. The degree of polymerization is reported in the range of 80–200 (Sun 1996). Hemicelluloses can be potentially used in various fields. These polysaccharides can be used as alternatives to the natural energy sources that are getting constantly depleted. They can also be used in their native or modified forms to form biocomposite films for the development of packaging materials (Li and Pan 2018). The chemically modified polysaccharide can potentially find use in various industries.

Hemicellulose exhibits poor solubility in common organic solvents and low thermal stability during sample processing. These properties result in poor compatibility between the hydrophilic hemicellulose chain and the hydrophobic polymeric matrix (Lönnberg et al. 2006; Huda et al. 2005). Hemicelluloses can be chemically modified due to the large number of hydroxyl groups present in the hemicellulose backbones. Esterification (acetylation, oleoylation, lauroylation, fluorination) and crosslinking (Peng et al. 2010) reactions can be carried out with the hemicelluloses. The compounds can also be chemically modified by carrying out etherification (methylation, carboxymethylation, benzylation) and hydrolysis (Alekhina et al. 2014; Ren et al. 2008a) reactions. The biodegradability, biocompatibility, and structural backbone characteristics are retained (Kong et al. 2018; Liu et al. 2019).

Hemicellulose is isolated from the cell walls of plant biomass prior to carrying out the chemical modification reactions. The difficulty in solubilizing hemicellulose, present in biomass, can be attributed to biomass recalcitrance (especially the interaction between the hemicellulose and cellulose (and/or lignin) components of the cell wall) and biomass heterogeneity (Melati et al. 2021). The alkaline solubilization and enzymatic solubilization processes can be used to isolate hemicellulose. Hemicellulose can also be isolated using peroxide-based reagents in an alkaline medium (Alves et al. 2020). The isolation methods can potentially affect the properties (such as the degree of polymerization) of hemicellulose. The side groups present in the backbone can also be affected by reacting in the isolation process altering the properties of the hemicellulose (Brienzo et al. 2009, 2016; Figueiredo et al. 2017).

The specific properties exhibited by hemicellulose after chemical modifications depend on the functional groups introduced, types of linkages formed, substitution patterns produced, and degree of substitution achieved. The modified hemicellulose can be used in a wide range of fields and for the preparation of materials with specific features (Salam et al. 2011).

The hydrophobicity, thermal stability, viscosity, and solubility (in various solvents such as chloroform, dimethylsulfoxide, and tetrahydrofuran) of hemicellulose can be tuned by derivatizing hemicellulose compounds. The biocompatibility, water resistance, and stability of the compounds against microorganisms were considered during derivatization. These properties make the modified hemicellulose molecules suitable for application in various industrial fields. They can be potentially used for the development of biodegradable films, hydrogels, medical implants, etc.

Solubilization of hemicellulose results in the formation of macromolecules (Martins et al. 2021). Partial hydrolysis of the compounds results in the formation of oligomers while total hydrolysis of hemicellulose results in the formation of monosaccharides (Forsan et al. 2021a; Freitas et al. 2021). Chemically modified hemicelluloses exhibit new properties that make the modified compounds suitable for specific applications. This review aims to investigate the possible chemical modifications that can be introduced into the structure of hemicellulose. The advantages and disadvantages of the methods used to chemically modify hemicellulose molecules have also been presented. The potential applications (based on the chemical modifications) of the molecules have also been discussed.

## 6.2 Solubilization of Hemicellulose

Hemicellulose is extracted from the lignocellulosic biomass (agro and industrial waste). Hemicelluloses are tightly bound to lignin and cellulose present in the plant cell wall. This results in the formation of microfibrils, which organize to form stable macrofibrils (Liu et al. 2016). Hemicellulose interacts with lignin through covalent bonds to form lignin–carbohydrate complexes that contain phenyl glycoside bonds, ester groups, and benzyl ether moieties (Schmatz et al. 2020; Christopher 2012). It is believed that hydrogen bonds are formed between hemicellulose and cellulose (Fig. 6.1) (Lodish et al. 2000).

Ester linkages are formed between acetyl units and hydroxycinnamic acids in hemicelluloses (Fig. 6.2) (Peng et al. 2012). The diverse nature of the bonds present in the molecules makes the isolation of hemicellulose from the plant cell wall difficult. Structural modifications (e.g., the reduction in the degree of polymerization) help in the efficient extraction of hemicellulose from plant cell walls (Brillouet et al. 1982; Sun et al. 2004).

The chemical composition and morphology of the wood matrix dictate the choice of the hemicellulose solubilization method. The use of the obtained carbohydrates and their potential for further valorization help in identifying the solubilization method to be followed (Yedro et al. 2017). Annual plants contain less amounts of lignin. Thus, it is easier to isolate hemicellulose from annual plants than from wood (Ebringerová and Hromádková 1999). The solubilization processes can cause significant modifications in the carbohydrate structure. Thus, the choice of the solubilization method depends on the potential use of the final product (Sjöström 1993;

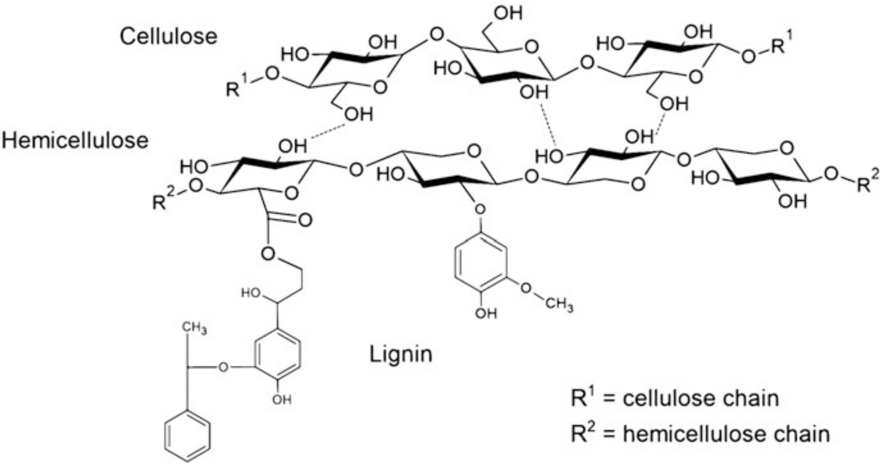


**Fig. 6.1** Hemicellulose-cellulose and hemicellulose-lignin linkages

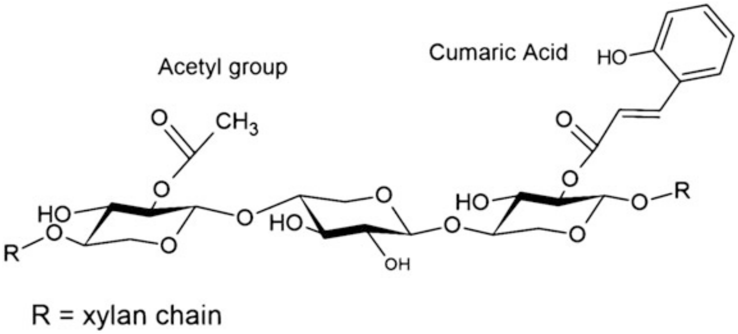


**Fig. 6.2** Hemicellulose containing pendant acetyl and cumaric acid groups

Yedro et al. 2017). In some cases, hemicellulose can be directly extracted from wood. In most cases, wood is first delignified to holocellulose, and hemicellulose is then extracted over one or several steps. Direct solubilization results in minimal chemical modifications.

The choice of the solubilization method influences the degree of polymerization and the process of monomer release. The solubilization method also dictates the nature of the degradation products and the type of substituents introduced into the hemicellulose scaffold. Methods like acid hydrolysis and steam explosion can be efficiently used to obtain hemicellulose in the form of monomers. The alkaline treatment and organic solvent solubilization methods result in the isolation of hemicellulose in the form of macromolecules that exhibit a high degree of polymerization. Pretreatment methods involving the use of hot water, steam, and acid result in the partial hydrolysis of hemicellulose, which results in the formation of oligomers.

## 6.2.1 Solubilization of Hemicellulose in the Form of High and Low DP

### 6.2.1.1 Alkaline Treatment Method

The linkages between hemicellulose and lignin are cleaved when the alkaline treatment method is used to treat lignocellulosic materials. The cleavage of the bonds results in the solubilization of hemicellulose (Brienzo et al. 2016) (Fig. 6.3). The alkaline treatment method is used to effectively solubilize lignin present in lignocellulosic biomass. The solubilization of lignin helps reduce enzyme impediment and increases the availability of polysaccharides for reactions (Shimizu et al. 2020). The process results in the hydrolysis of uronic and acetic esters and swelling of cellulose. The cellulose crystallinity can decrease due to the alkaline treatment (Shimizu et al. 2018; Melati et al. 2019; Brienzo et al. 2016). The *O*-acetyl groups are cleaved and acetic acid is released. Experimental conditions of high pH are

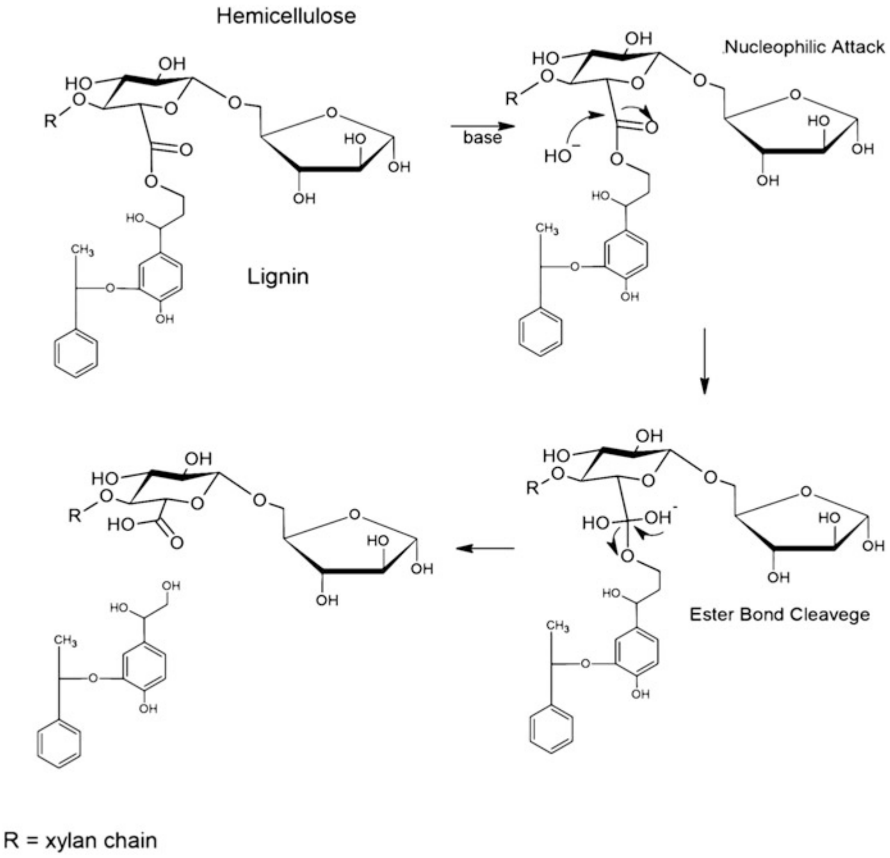


**Fig. 6.3** Linkages between hemicellulose and lignin are broken under alkaline conditions

responsible for the deacetylation (Peng et al. 2012). The glycosidic bonds cannot be broken under moderate reaction conditions to hydrolyze hemicellulose molecules to form monomers. Therefore, the alkaline treatment method (NaOH or KOH is used) can be used to obtain hemicellulose with a high degree of polymerization (Brienzo et al. 2016; Alves et al. 2020).

The use of hydrogen peroxide in the alkaline treatment method promotes delignification and solubilization of hemicelluloses (Brienzo et al. 2009) present in lignocellulosic materials. Hydrogen peroxide is highly reactive and exhibits strong oxidizing ability (Dutra et al. 2017). Hydrogen peroxide dissociates to produce hydroperoxide anions (HOO−) which react with hydrogen peroxide in an alkaline medium to form hydroxyl radicals ($OH^-$) and superoxide anion ($O_2{}^-$) that oxidize lignin. Hydrophilic (carboxyl) groups are introduced into the scaffold and interunit bonds are cleaved resulting in the dissolution of lignin and hemicellulose (Dutra et al. 2017).

The alkaline treatment method can be used to solubilize hemicellulose present in poplar. The sample is treated for 3 h at a temperature of 50 °C. The liquid to solid ratio was 20:1. NaOH solution (10%, (w/w)) was used to solubilize hemicelluloses (solubilization yield of xylan: 71.8%; solubilization yield of galactan: 6.3%; solubilization yield of arabinan and mannan sum: 11.9%). The degree of polymerization was 167 (Geng et al. 2018). The efficiency of solubilization can be increased by delignifying poplar prior to subjecting it to the alkaline treatment method as NaOH solution cannot effectively react with hemicellulose in the presence of lignin. The alkaline solubilization method resulted in the solubilization of xylan (solubilization yield: 90.1%), galactan (solubilization yield: 18.8%), arabinan (solubilization yield: 25.4%), and mannan (solubilization yield: 25.4%). The degree of polymerization was 89 (Geng et al. 2018). NaOH solution (10%; reaction condition temperature: 50 °C; reaction time: 3 h) was used to extract hemicellulose (degree of polymerization: 392) from partially delignified switchgrass. The solubilization yield was calculated to be 22% (Farhat et al. 2016).

An alkaline solubilization method that involves the use of peroxide was proposed for solubilizing xylan. The pH was adjusted using sodium hydroxide and xylan was extracted from sugarcane bagasse with varying mesh sizes. The amount of residual lignin was the least (4.40%) in the xylan solubilized from 50 mesh-sugarcane bagasse. The xylan solubilization yield was found to be 64.67%. The minimum xylan solubilization (31.18%) was recorded with 16 mesh-sugarcane bagasse (i.e., with sugarcane bagasse exhibiting high granulometry). The amount of residual lignin in the xylan was the maximum (6.19%) in this case (Alves et al. 2020). Highly soluble xylan was obtained (>96% solubility) that is positive for further polysaccharide application such as could be enzymatically hydrolyzed to produce xylooligosaccharides (Alves et al. 2020).

#### 6.2.1.2 Liquid Hot Water Treatment Method

The liquid hot water treatment method hydrolysis of the acetyl group present in hemicellulose, resulting in the formation of acetic acid (in solution) that is the catalyst in the treatment. The deacetylation of the xylan side chain during the pretreatment process results in the production of acetic acid. Consequently, $H_3O^+$ ions are produced, resulting in a decrease in the pH of the system. Under these conditions, self-hydrolysis of xylan occurs. This method can be effectively used to selectively obtain hemicellulose oligomers over monomers. Degradation of monosaccharides can be avoided as moderate reaction conditions are used (Gallina et al. 2017).

The method involves cooking raw materials, using water as the solvent, in the temperature range of 130–180 °C to obtain an aqueous solution of hydrolyzed xylan (Liu et al. 2019). The use of water makes the process environmentally friendly and economically viable. At high temperatures as extreme reaction conditions can potentially lead to the hydrolysis of polysaccharides, resulting in the formation of monomers. Therefore, it is important to regulate the reaction temperature to predict the degree of polymerization. The solubilization yield increases and the degree of polymerization decreases with an increase in the reaction temperature (Gallina et al. 2017).

With a flow-through reactor operated at 160 °C for 90 min (pressurized at 11 bar) under conditions of liquid hot water treatment method, 33.9% of hemicellulose (molecular weight: 1922 Da; degree of polymerization: 14.54) present in catalpa wood was solubilized (Gallina et al. 2017). The solubilization yield was recorded to be 41.7% when the temperature was increased to 170 °C. The molecular weight was 1417 Da and the degree of polymerization was 10.72 (Gallina et al. 2017). The amount of hemicellulose hydrolyzed increased with increasing temperature. This resulted in the detachment of the oligomers from the matrix and a decrease in the oligomer size. Thus, the molecular weight decreased with increasing temperature (Gallina et al. 2017).

The liquid hot water treatment method has been used to solubilize arabinoxylan (degree of polymerization: 68.11) present in wheat bran. The process was catalyzed by ruthenium (III) chloride supported by mobil composition of matter n° 48 impregnated with aluminum ($RuCl_3$/Al-MCM-48) (reaction condition: 180 °C/10 min). The pretreatment method involved destarching the wheat bran, with the solubilization yield recorded of 78% (monosaccharide yield: 15%). When the temperature was decreased to 160 °C and MCM-48 was used as the catalyst, compounds of higher molecular weight (65.2 kDa) were obtained. The degree of polymerization was 493.45. The solubilization yield decreased (24%) and the monosaccharides yield was $<10\%$ (Sánchez-Bastardo et al. 2017). Therefore, the degree of polymerization of hemicellulose (obtained following the liquid hot water treatment) may be partially controlled in regard to treatment conditions, such as temperature and presence of a catalyst.

The effect of the treatment conditions on the solubilization yield was studied when the liquid hot water treatment method was used to treat holm oak sapwood. The maximum yield of 59.47% was obtained when the solubilization process was carried out at a temperature of 170 °C for 20 min. The highest degree of polymerization was recorded when the reaction time was the shortest. The degree of polymerization decreased as the reaction time increased. The maximum average molar mass was 12.9 kDa when the treatment was conducted at 170 °C for 5 min (degree of polymerization: 97.6). The lowest average molar mass of 1.8 kDa was obtained when the sample was treated at a temperature of 170 °C for 60 min (degree of polymerization: 13.62) (Yedro et al. 2017).

#### 6.2.1.3 Organic Solvent Treatment Method

The organic solvent treatment method can be used to isolate hemicelluloses. The scarcity of knowledge on the dynamic solvent effects limits the practical application of the method (Baig et al. 2019). The organic solvent treatment method involves the use of low-boiling organic solvents such as ethanol, methanol, butanol, and acetone. The process can be carried out at low temperatures in the presence of alkaline catalysts such as sodium hydroxide and potassium hydroxide for biomass fractionation (Mesa et al. 2011; Guragain et al. 2016).

The alkali-catalyzed organosolv process can be used to selectively cleave covalent bonds (α ester linkages) between hemicelluloses and lignin present in the cell wall matrix. The polymeric form of hemicellulose is maintained. The process of fractionation of biomass also results in the cleavage of uronic acid and arabinose side chains (Liu et al. 2016; Geng et al. 2018; Peng et al. 2012). The solvents used in the organic solvent treatment method can be recovered by distillation. The process probably does not significantly impact the environment as it is a low energy consumption process (extremely high temperatures are not required) (Pan et al. 2006; Vila et al. 2003). However, a large volume of wastewater is needed to wash the resulting material. This limits the economic viability of the process (Laure et al. 2014; Baig et al. 2019). Precautions need to be taken during the process as some organic solvents are inflammable, combustible, toxic, and/or hazardous. This increases the operational cost of the method (Baig et al. 2019). However, this process has been already used for biomass delignification.

Hemicellulose obtained from flax shives was solubilized using pressurized aqueous ethanol (solubilization yield: 81%; reaction temperature: 180 °C; reaction time: 117 min; pressure: 5.2 MPa). A high degree of polymerization was observed in 47% of the solubilized hemicellulose (Buranov and Mazza 2010). An ethanol/water solution (50%, v/v) was used during the organosolv pretreatment method to solubilize hemicellulose present in sugarcane bagasse. The treatment was carried out at a temperature of 190 °C. The reaction time was varied and the maximum amount of hemicellulose was solubilized when the solubilization reaction was carried out for 100 min. The sample was pretreated following the hydrothermal method prior to conducting the organosolv pretreatment process. It was observed that the maximum hemicellulose solubilization could be achieved if only the organosolv pretreatment method was followed to treat the samples (Espirito Santo et al. 2018).

#### 6.2.1.4 Enzymatic Solubilization Process

Numerous bacteria and fungi have the natural ability to enzymatically hydrolyze lignocellulosic biomass to obtain nutrients (Janusz et al. 2017). Large biopolymers cannot efficiently penetrate the cells of such microorganisms. The microorganisms secrete a mixture of enzymes that break polymers into smaller soluble oligomers.

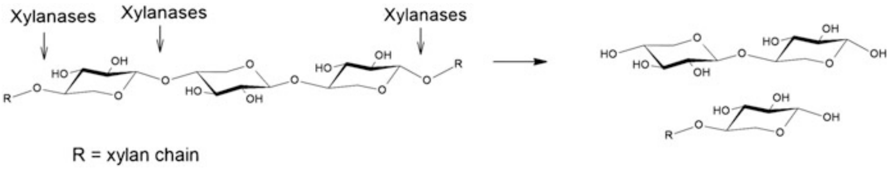


**Fig. 6.4** Enzyme-based solubilization of hemicellulose

These smaller oligomers can be efficiently transported into the cells where they get metabolized (Fig. 6.4) (Luo et al. 2002).

The enzymatic hydrolysis processes involve the use of specific hemicellulose enzymes that hydrolyze hemicellulose to produce hemicellulose derivatives. The enzymatic hydrolysis process is slower than the previously discussed processes of hydrolysis. The degree of polymerization can be controlled by the reaction time and enzyme activity. Monomers or degradation products are not released or formed in the enzymatic process (Freitas et al. 2019). The original structure and activity of hemicellulose are retained. The enzymatic hydrolysis processes are more environmentally friendly than the chemical hydrolysis processes (Escarnot et al. 2012).

The enzymes need to penetrate the cell wall to efficiently react with hemicellulose. Lignin, present in the cell wall, hinders the reaction between enzymes and hemicellulose. Thus, the efficiency of the enzymatic process depends on the composition of the biomass used (Shimizu et al. 2020). A pretreatment method that does not affect the hemicellulose structure is followed to remove lignin. Chemicals (such as sodium chlorite and peracetic acid, at lab scale) are used to achieve delignification and bleaching (Hakala et al. 2013; Geng et al. 2018).

Xylanase, obtained from *Thermomyces lanuginosus*, was used to hydrolyze xylans. The use of bulk aqueous, organic, or inorganic solvents was avoided and hemicellulose present in chemically untreated biomass was directly hydrolyzed. Soluble xylooligosaccharides (with a low degree of polymerization) were obtained (sugarcane bagasse: 73% yield; wheat straw: 84% yield) when hydrolysis reactions were carried out for 72 h at a temperature of 55 °C in the presence of xylanase. The samples were ball milled for 30 min prior to conducting the hydrolysis reactions (Ostadjoo et al. 2019).

Approximately 22% of xylan present in wheat straw was solubilized following the xylanase pretreatment process (treatment conditions: 60 °C/6 h) conducted using 350 IU/g of straw. An increase in the xylanase load did not result in improved xylan solubilization. However, when the xylanase pretreatment process was conducted for 24 h (after soaking the biomass in aqueous ammonia (30%, v/v) for 3 days), 56% of the xylans could be hydrolyzed into xylose, xylobiose, and xylotriose (Rémond et al. 2010). Longer reaction times did not result in an increased extent of solubilization. The process could be used to successfully cleave the ester linkages in phenolic acids (present in the xylan chains), and 60% and 76% of *p*-coumaric and ferulic acids were removed, respectively.

Biomass was pretreated following an alkaline-sulfite chemi-thermomechanical process to facilitate the solubilization of xylan (using the enzymatic or alkaline treatment procedures). The enzymatic solubilization process was carried out in the presence of commercial xylanase (dosage: 8 IU/g of pretreated bagasse). A yield of 22% (w/w; xylan solubilization yield) was observed (molecular weight: <6 kDa; degree of polymerization: <45.41). The process could be used to obtain xylan contaminated with less amounts of lignin and glucan (lignin: <4%; glucan: <2.2% in the final solid biomass) (Sporck et al. 2017). The enzymatically extracted xylan exhibited a high substitution degree (primarily substituted by uronic acid groups), resulting in high water solubility. This material can be deposited onto cellulosic pulps to increase the xylan content. Thus, the importance of xylan from bagasse can be potentially increased (Sporck et al. 2017).

A combination of xylanase and cellulase can result in improved hemicellulose hydrolysis. Destarchment and deproteinization processes were conducted prior to conducting the solubilization processes used to solubilize hemicellulose (present in oat bran) in the presence of enzymes. The biomass components were not separated prior to the solubilization processes. Various combinations of enzymes were tested and the reaction times were varied. The maximum solubilization yield of 69.7% (for arabinoxylan) was obtained when a commercial cellulolytic preparation treatment method was followed (treatment conditions: 55 °C/24 h) and endoxylanase was used. The degree of polymerization was in the range of 1–1151. Approximately 50.3% of the molecules were extracted in the form of monomers (Escarnot et al. 2012).

### 6.2.2 Solubilization of Hemicellulose in the Form of Monosaccharides

#### 6.2.2.1 Acid hydrolysis Method

The acid hydrolysis process of solubilizing hemicellulose involves the use of a concentrated or dilute acid that can help break the linkages present between biomass components. The process results in the fragmentation/hydrolysis of hemicelluloses into their constitutional pyranose and furanose sugar units. During the hydrolysis process, the added acid dissociates, releasing protons, and diffuses through the biomass pore spaces to reach the reactive sites. The released protons subsequently catalyze the cleavage of the acetyl groups present in the hemicellulose chains. The acidity of the medium increases during the process (Fig. 6.5) (Stella Kapu and Trajano 2014). The monosaccharides are obtained in high yields. The yields depend on the reaction conditions used. Oligomers and monosaccharides are obtained as the products (Forsan et al. 2021b; Brienzo et al. 2016).

During this process, the acid penetrates the cell wall and causes the degradation of lignin, which physically hinders access to the polysaccharides. The rate of hemicellulose hydrolysis is the fastest when the acid hydrolysis method is used to hydrolyze hemicellulose. The rate is slower when the enzyme solubilization and liquid hot

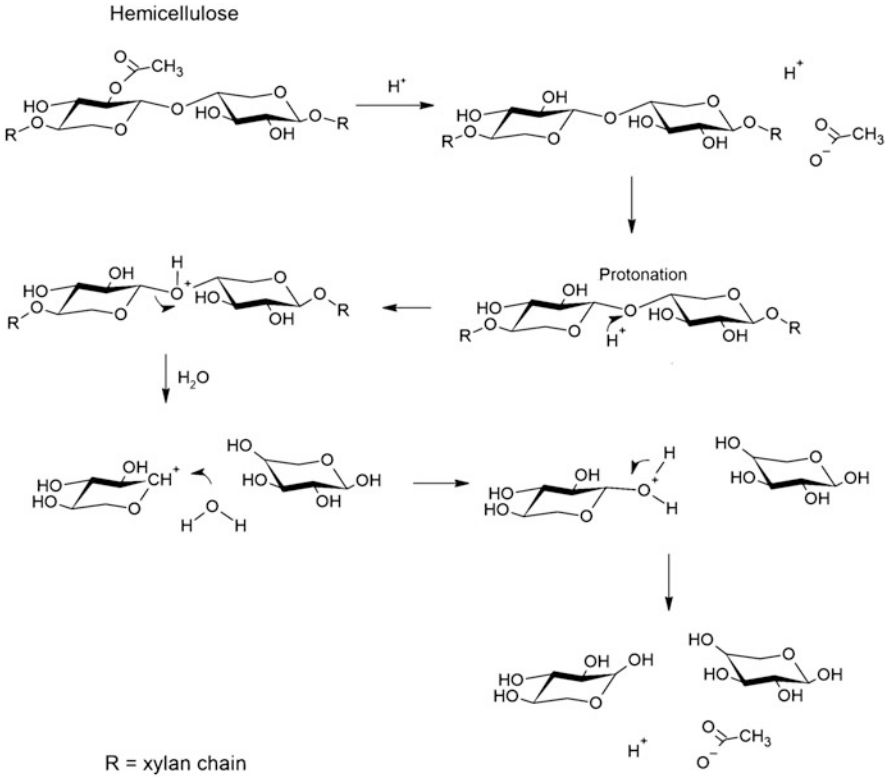
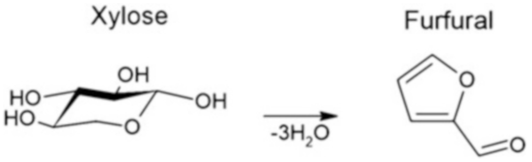


**Fig. 6.5** Acid-catalyzed hydrolysis of hemicellulose

**Fig. 6.6** Xylose dehydration to form furfural



water treatment method are used for hydrolysis (Melati et al. 2019; Goldmann et al. 2017).

The acid hydrolysis method can potentially lead to the degradation of sugar molecules. Furfural is produced when xylose is dehydrated under harsh reaction conditions (Fig. 6.6). Acid insoluble pseudo-lignin is formed when aromatic compounds are formed from the structural rearrangement of furfural and lignin fragments repolymerize (Hu and Ragauskas 2012; Schmatz et al. 2020). Furfural and acetyl compounds function as microorganism inhibitors when hemicellulose hydrolysate is fermented. This results in reduced fermentation process efficiency

(Candido et al. 2020). The yields of the inhibitors increase when hydrolysis is conducted under conditions of high temperatures and acid concentrations (harsh solubilization conditions) (Candido et al. 2020). When the reactions are conducted in the presence of concentrated acid, corrosion-resistant equipment should be used. The acid can be recovered following the completion of the hydrolysis process.

Hemicellulose present in poplar wood was solubilized using a binary solvent composed of formic acid and water (formic acid fraction: $<77.5\%$ (w/w) of azeotrope). The reaction times and reaction temperatures were varied. The maximum hemicellulose yield was obtained when the reaction was carried out at a temperature of 120 °C and the reaction time was 1 h (arabinose: 93.5%; xylose: 77.8%; mannose: 94.5%, and galactose: 97.9%) (Xu et al. 2018). The yields of all the hemicellulose-derived saccharides increased when the solubilization time was increased. The reactions (especially with mannose and galactose) were carried out in the temperature range of 90–100 °C. The yields decreased as the solubilization times increased when the temperature was 120 °C. This can be attributed to the fast rate of degradation of the saccharides, the rate of degradation was the maximum when the temperature was 140 °C (Xu et al. 2018). As the solubilization time increased, the mass loss of xylan increased. The maximum mass loss was recorded to be 18.57% after 10 h. This indicated that substantial amounts of intermediates were formed during the conversion of hemicellulose-derived saccharides to furanic compounds. The results also indicated that side condensation reactions occurred between the intermediates and the furfural or lignin-derived compounds (Xu et al. 2018).

Hemicellulose was extracted from birch (*Betula pendula*) sawdust using formic acid and hot water. Solubilization experiments were carried out under various reaction conditions. The maximum xylose yield (47.53% xylose (w/w); reaction condition: 140 °C/2 h) was obtained using 7.24% (w/w) of formic acid (Goldmann et al. 2017). The experimental results revealed that the maximum rate of hemicellulose degradation, leading to the formation of furfural, was recorded when the rate of degradation of hemicellulose increased as the reaction temperature and reaction time increased. The yield of xylose decreased with increasing reaction time when the reaction temperature was 170 °C. The concentration of formic acid did not influence the yield as xylose was dehydrated to form furfural (Goldmann et al. 2017).

The reaction was conducted over a short period of time under conditions of low temperature in the presence of sulfuric acid. The process resulted in the recovery of 83.5% of xylose when the samples were pretreated with sulfuric acid (35 mmol/L; treatment conditions: 170.05 °C/12 min). The degradation of xylose to form furfural and hydroxymethylfurfural under such moderate reaction conditions could be avoided (Diedericks et al. 2013).

#### 6.2.2.2 Steam Explosion Method

The method of steam explosion is used for biomass conversion, with effect in partial hemicellulose solubilization. The auto-hydrolysis reaction results in the physical rupture of the biomass cell wall. The penetration of high-pressure steam into the plant cell walls leads to abrupt decompression, resulting in the physical rupture of the cell walls (Baig et al. 2019). As the pressure increases, steam starts to penetrate the biomass material. The vapor condenses, leading to the moistening of the biomass. At high temperatures, the condensed water (present inside the material) reacts with hemicellulose and induces the hydrolysis of the acetyl and methylglucuronic groups. Acetic acid and uronic acid are produced, resulting in a decrease in the pH of the medium. The acids catalyze the depolymerization reaction (Jacquet et al. 2010). In the next step, a sudden drop in the pressure is observed. A fraction of the water present in the material condenses and promotes the rupture of the plant cell wall of the raw materials (Jacquet et al. 2010; Grous et al. 1986). Centrifugation or filtration methods can be used to remove insoluble matter (such as cellulose) from the system. The hydrolysate containing the hydrolyzed hemicellulose and lignin fragments is obtained (Grous et al. 1986).

Water is the only reagent utilized in this simple process. Acid catalysts such as $SO_2$ or $H_2SO_4$ should be used to pretreat softwood materials such as pine. It is more difficult to autohydrolyze softwood materials (compared to agricultural residues and hardwoods) (Negro et al. 2003). The use of acid catalysts makes the reaction conditions harsh. Under these conditions, hemicellulose can be extracted in the form of monomers and degradation products such as furfural and hydroxymethylfurfural (glucose degradation) are formed. The solubilization yield decreases when xylose is degraded. The results reveal that the steam explosion method is unsuitable for the extraction of polymeric hemicellulose (Mihiretu et al. 2019).

The steam explosion method is regarded as one of the most cost-effective pretreatment processes that can be used to treat hardwoods and agricultural residues (Ge et al. 2017). The installation cost is high. However, it was found to be the most efficient pretreatment method with an internal rate of return of 28.04% (Nieder-Heitmann et al. 2019). The steam explosion method is an environmentally friendly and easy-operate method. It is one of the most efficient pretreatment methods that can be used for fractionating lignocellulosic materials (Melati et al. 2019). However, the operation conditions lead to the hydrolysis of hemicellulose present in biomass. Thus, the steam explosion method should be used to obtain hemicellulose in the form of oligomers or monosaccharides.

Sulfuric acid was used as a catalyst in the steam explosion method to solubilize hemicellulose present in slash pine sawdust. The maximum efficiency was recorded when the process was carried out at a temperature of 200 °C and the reaction time was 5 min (sulfuric acid: 3% (w/w); solubilization yield: 90%). The steam explosion method carried out under mild conditions results in low solubilization yield and high degrees of polymerization. Hemicellulose is extracted as oligomers. However, under harsh reaction conditions, hemicellulose was isolated predominantly in the form of monosaccharides and they were present in the corresponding pretreatment liquors (Stoffel et al. 2017). A lower solubilization yield of 51% was recorded under similar steam explosion conditions (204 °C/10 min). In this case, steam explosion was used to solubilize hemicellulose present in sugarcane, and sodium hydroxide was used as the catalyst (Mihiretu et al. 2019).

Under severe conditions, the maximum solubilization yield was recorded to be 19.4% when hemicellulose present in spruce sawdust was hydrolyzed in the presence of sodium hydroxide (catalyst). Low molecular weight products with low degrees of polymerization were obtained. High molecular weight compounds were obtained when the hydrolysis was carried out under milder reaction severity conditions (Chadni et al. 2019).

Xylan was depolymerized to form xylose that was subsequently dehydrated to form furfural when the steam explosion biomass treatment method was used for solubilization. Structural rearrangement in furfural with lignin derivatives resulted in the formation of pseudo-lignin. Harsh treatment conditions can potentially lead to the accumulation of pseudo-lignin and degradation products (Sannigrahi et al. 2011).

## 6.3 Chemical Modifications of Hemicellulose

Hemicellulose can be chemically modified to produce compounds with novel properties. The structurally modified hemicellulose molecules can find their applications in specific fields. The solubility and thermal stability of the compound can be improved by tuning the structural characteristics. The biodegradability, biocompatibility, and core structural features remain unaltered (Kong et al. 2018). The hydroxyl groups present in the backbones of the hemicellulose molecules can be chemically modified. Thus, the ease of modification depends on the number of hydroxyl groups present. Various carbohydrates (such as cellulose and starch) that are available in the form of residues have been chemically modified. These polysaccharides contain three hydroxyl groups in each monomer, while hemicelluloses contain only one or two hydroxyl groups that can be chemically modified. Thus, it is more difficult to chemically modify hemicellulose and easier to modify cellulose and starch (Fang et al. 1999).

Numerous methods have been developed over the years for the production of hemicellulose derivatives. The esterification and etherification reactions help introduce functional groups into the polysaccharide chains.

### 6.3.1 Hemicellulose Esterification

Alcohols and carboxylic acid (or derivatives of carboxylic acids such as acid chlorides and acid anhydrides) groups react to form esters. Esterification reactions have been conducted to produce modified hemicellulose molecules. The hydrophobicity, solubility, and thermal processability of the modified hemicellulose derivatives are different than those of the parent hemicelluloses. Hemicellulose-based biodegradable films, paper coatings, medical implants, and hydrogels have been reported (Fundador et al. 2012; Fang et al. 1999; Belmokaddem et al. 2011).

The first step of the esterification reaction involves a nucleophilic attack on the carbonyl carbon atom of the carboxylic acid molecule. The OH group of the sugar molecule acts as the nucleophile. The lone pair of electrons on the OH group attacks the carbonyl carbon. The leaving group departs, resulting in the formation of esterified hemicellulose. This is often an acid- or base-catalyzed reaction (Fig. 6.7). Researchers have used different solvents and catalysts to produce

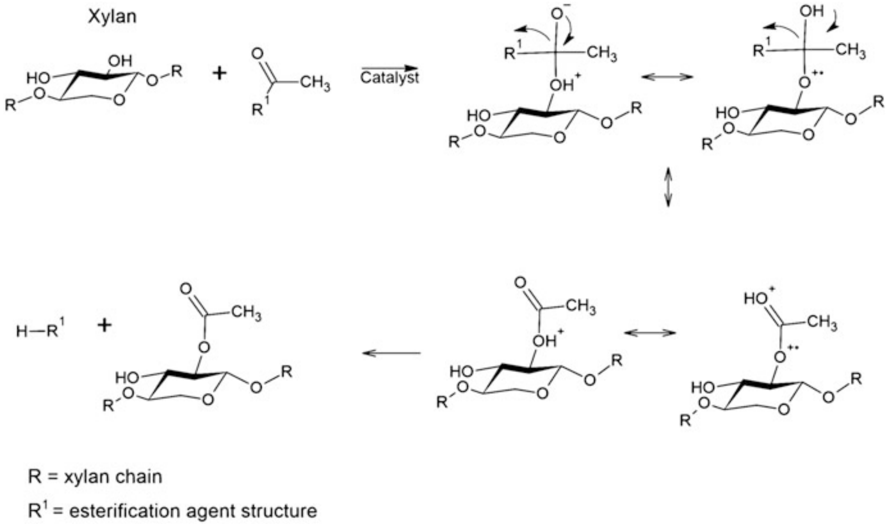


**Fig. 6.7** Esterification pathway of hemicellulose

hemicellulose esters (Gröndahl et al. 2003; Mugwagwa and Chimphango 2020a; Stepan et al. 2013; Renard and Jarvis 1999).

Recently, ionic liquids (ILs) have gained immense attention and have been used as reactive solvents for esterification as they are eco-friendly, recyclable, and highly reactive. They also exhibit enhanced thermal stability and low viscosity. Negligible vapor pressure is produced at room temperature when ILs are used (Wu et al. 2004; Barthel and Heinze 2006; Heinze et al. 2005). ILs are commonly defined as salts that are in their molten states at temperatures below 100 °C. They can dissolve complex macromolecules and polymeric materials. Carbohydrates can be efficiently dissolved in ILs with high efficiency and are regarded as clean solvents that can be used in chemical reactions (Moens and Khan 2003). Such solvents help break the extensive hydrogen-bonding network and promote the dissolution of polysaccharides (Swatloski et al. 2002).

The esterification reaction is one of the most versatile reactions that can be used to achieve structural modifications in hemicellulose molecules to make them suitable for industrial applications. For example, polysaccharides are modified to produce films that can replace plastic. Hemicelluloses containing one or two hydroxyl groups are hydrophilic in nature and synthetic polymers are hydrophobic in nature (Fang et al. 1999).

Esterified polysaccharides (acetylated cellulose, acetylated xylan, acetylated starch, starch propionate, starch butyrate, starch valerate, and starch hexanoate) can be used to reduce the anaerobic biodegradation of bioplastic. When the degrees of substitution of starch, cellulose, and acetylated xylan were >1.5, 1.5, and 1.2, respectively, the biodegradation of bioplastic was hindered (Rivard et al. 1995).

The lignocellulosic fibers (hemicellulose and lignin) of different vegetables were chemically modified (esterified) to yield materials exhibiting enhanced surface adhesion properties (Tserki et al. 2005). The thermal stability, crystallinity, and hydrophilicity of the modified fibers decreased. The modified fiber/polyester composites exhibited decreased fiber hydrophilicity and water absorption properties (Tserki et al. 2005) that could potentially affect the biodegradation processes (Tserki et al. 2006). These modified fibers could be used to reduce the rate of biodegradation of esterified lignocellulosic fibers (Tserki et al. 2006). The rate of biodegradation decreased as the bioplastics could not efficiently interact with water as the OH groups present in the fibers were replaced by ester groups. Therefore, the extent of diffusion of water through the composite and the rate of biodegradation were affected.

#### 6.3.1.1 Acetylation

Hemicellulose contains acetyl groups in its chains. The nature of the acetylated polymer and the extent of acetylation differ between plant species, plant tissues, and types of plant cell walls (Pawar et al. 2013). The xylans from graminaceous plants, for example, contain 1–2% acetyl pending groups. Deacetylation occurs when the hemicellulose molecules are solubilized in an alkaline medium. The resulting products are highly hydrophilic as they bear a large number of hydroxyl groups.

The acetylation reaction (an esterification reaction) helps introduce acetyl groups into the hemicellulose backbone (Fig. 6.8). Schuetzenberger was the first to synthesize carbohydrate acetates (in 1865) using acetic anhydride (Davis 1929; Schuetzenberger 1865).

The increase in hydrophobicity of the compounds can be attributed to the acetylation of the hydroxyl groups present in hemicelluloses. Acetylation hinders the formation of hydrogen bonds (between hydroxyl groups and water molecules), resulting in increased water resistance. These properties make the hemicellulose derivatives suitable for application in various fields (Mugwagwa and Chimphango 2020a). The formation of intermolecular hydrogen bonds in hemicelluloses is hindered.

The degree of acetylation dictates the hydrophobicity of the acetylated hemicelluloses. The non-acetylated xylan (degree of acetylation: 0) is partially soluble in hot water. The partial solubility can be attributed to the spontaneous intra-molecular hydrogen bonding, possibly resulting in the formation of a crystalline network. The partially acetylated xylan (degree of acetylation: ~0.5) is fully soluble in water. The high solubility can be attributed to the presence of the free

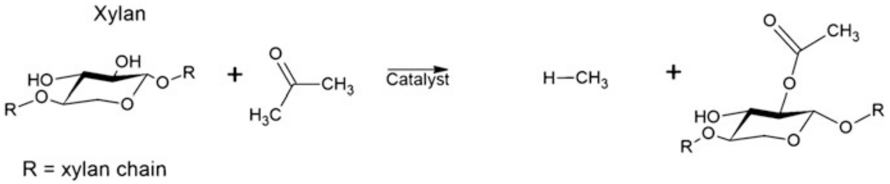


**Fig. 6.8** Reaction representing the acetylation of hemicellulose

hydroxyl groups in the hemicellulose chain. Xylan molecules in which all the hydroxyl groups have been acetylated (degree of acetylation: 2) dissolve in non-polar solvents like chloroform and polar aprotic solvents like dimethyl sulfoxide (Stepan et al. 2013). The solubilities of the acetylated hemicelluloses in organic solvents such as chloroform, dimethylsulfoxide, and tetrahydrofuran increase with the increase in the degree of substitution (degree of acetylation) (Sun et al. 1999).

Numerous acetylation methods have been reported that can be used to achieve varying degrees of substitution. These methods can also be used to produce different patterns of properties. However, the most common reaction used to acetylate hemicelluloses involves the use of acetic anhydride as the reagent. The gas-phase surface esterification and plasma treatment-assisted surface esterification reactions can be conducted to acetylate hemicelluloses. The samples can be pretreated with glacial acetic acid to achieve different levels of acetylation (Berlioz et al. 2009). The use of ionic liquids as the medium has shown great potential for the direct dissolution of hemicellulose. This hemicellulose can be completely acetylated in a short period of time a high molecular weight can be retained (Stepan et al. 2013).

Acetylated hemicellulose is often the primary polymer component of films. However, hemicellulose can be used as a copolymer (with polycaprolactone) for the preparation of active packaging units. The film solubility reduced to 82% when acetylation of hemicellulose was carried out using acetic acid as the acetyl donor and sulfuric acid as the catalyst (Mugwagwa and Chimphango 2020a). The solubilities (in the fatty food simulants) of the acetylated hemicellulose films were lower (solubility as low as 12.57%) than the solubility of the polycaprolactone films and low-density polyethylene films (Mugwagwa and Chimphango 2020a). The degree of substitution was in the range of 0.59–1.25 and enhanced thermal stability could be achieved when acetylation of wheat straw hemicellulose was carried out in a homogeneous organic solvent system consisting of *N*,*N*-dimethylformamide and lithium chloride. Acetic anhydride was used as the esterification agent and 4-dimethylaminopyridine was used as the catalyst (Fang et al. 1999). A similar method was followed for the acetylation of arabinoxylan, where formamide was used as the solvent (single solvent) and pyridine was used as the catalyst. The resulting material was used for film production (Egüés et al. 2014). The film formed with acetylated arabinoxylan exhibited increased thermal stability. The maximum weight loss was achieved at a temperature of 375 °C, indicating a decrease in the number of hydroxyl groups. The hydroxyl groups get oxidized during heating (Egüés et al. 2014; Fundador et al. 2012). Acetylation resulted in increased tensile strength (elongation at break: 13.4%; Young's modulus: 2241 MPa). Internal plasticization of the acetyl groups resulted in improved elongation (Egüés et al. 2014).

Hemicellulose present in softwood biomass could be directly acetylated. The sample was not impregnated with acetic anhydride at 120 °C prior to solubilization (Sun et al. 2019). The percent of weight gain, which varied from 13.6% (reaction time: 30 min) to 22.3% (reaction time: 8 h), helped determine the acetylation efficiency.

A maximum weight gain of 22.7% was recorded when the acetylation reaction was carried out using acetic anhydride in the absence of catalysts and solvents. The reaction temperature was 120 °C and the reaction time was 4 h. The reaction was carried out in the presence of potassium acetate that was produced during the alkaline solubilization method. The water solubility decreased from 46% to 2.4% and the moisture content decreased from 63% to 12% upon acetylation. The results revealed that this easy-to-operate, efficient, cost-effective, and environmentally friendly method can be used to acetylate xylans in the absence of toxic catalysts (Akkus et al. 2018).

The alkali-based organosolv treatment method can be used (prior to hemicellulose solubilization) to optimize the acetylation reaction conditions (acetylation of hemicellulose present in wheat straw). Acetic acid was used as the acetylation agent and sulfuric acid was used as the catalyst. To obtain the optimum yield, the reaction was carried out for 1 h at a temperature of 50 °C (Mugwagwa and Chimphango 2020b). The organosolv treatment conditions were varied to determine the degree of acetylation of hemicellulose. The acetylated hemicellulose was used to produce films. The value of the water contact angle indicated the extent of hydrophobicity. When the organosolv treatment method (reagents: 80% ethanol and 1% NaOH; treatment time: 4 h) was used to treat the sample, the degree of substitution was recorded to be 1.7. The treated sample did not produce the most hydrophobic hemicellulose-based film (contact angle: 31.34°). The most hydrophobic hemicellulose-based film (water contact angle: 64.22°) was produced when the organosolv treatment method (reagents: 65% ethanol and 13% NaOH; treatment time: 2 h) was used to acetylate hemicellulose (degree of substitution: 0.45). The results confirmed that the hydrophobicity of hemicellulose did not solely depend on the degree of acetylation (Mugwagwa and Chimphango 2020b).

Numerous types of ILs can be used during acetylation. The acetylation reactions in ILs can be conducted in the presence or absence of catalysts. Hemicellulose present in switchgrass was acetylated using acetic anhydride in 1-allyl-3-methylimidazolium chloride in the absence of a catalyst. This method of acetylation was environmentally friendly and was used to produce hemicellulose acetate with a high degree of polymerization. The produced hemicellulose can be used in various industrial applications (Ayoub et al. 2013).

The hydrophilicity of the acetylated polysaccharides (starch, cellulose, and xylan) decreased as the degree of substitution increased. The enzymatic degradability also decreased with increasing degrees of substitution (Glasser et al. 1995). It is worth mentioning that in addition to the modifying polysaccharides and solubilization methods process, other factors such as type of enzyme, pH, and microorganisms must be considered in the enzymatic and microbiological degradation of bioplastics composed of modified polymers. It was reported that acetylated xylan did not hinder the process of degradation when the degree of substitution was in the range of 0–0.8 (Mitchell et al. 1990).

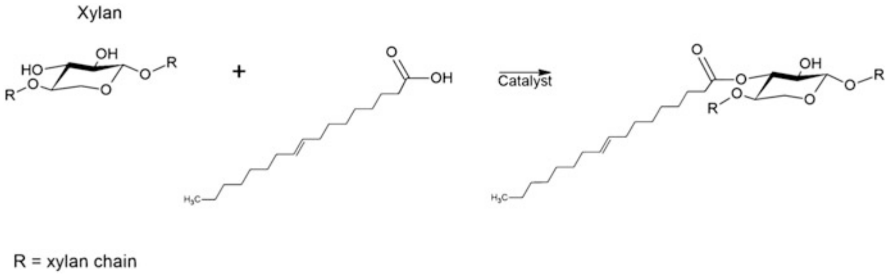


**Fig. 6.9** Reaction representing oleoylation of hemicellulose

### 6.3.1.2 Oleoylation

Oleoylation is a type of esterification reaction. The oleoylation reaction is conducted to convert the hydroxyl groups to oleoyl esters. Hydrophobic oleoyl groups are introduced into the scaffold (Fig. 6.9). The hemicellulose molecules are modified using a catalyst such as *N*-bromosuccinimide (or 4-dimethylaminopyridine). The *N*, *N*-dimethylformamide/lithium chloride system is used as the solvent system to conduct the reaction under mild conditions (Sun et al. 1999, 2004).

Oleoylation alters the water solubility of hemicellulose. The solubility of the compound in different organic solvents such as pyridine, tetrahydrofuran, toluene, and chloroform (Sun et al. 1999) increases, indicating increased hydrophobicity. The decrease in the thermal stability of hemicellulose (post oleoylation) can be attributed to the absence of intermolecular hydrogen bonds between the polymeric chains of hemicellulose in the unmodified polymer matrix (Sun et al. 2004).

Sugarcane bagasse hemicellulose was oleoylated, the degree of substitution was found to be 0.04. The thermal stability increased and the thermal degradation of the material was initiated at 187 °C. The unmodified hemicellulose started to decompose at 200 °C (Sun et al. 2004). When 4-dimethylaminopyridine was used as the catalyst and triethylamine was used as the neutralizer in a homogeneous solvent system composed of *N*,*N*-dimethylformamide and lithium chloride, >90% oleoylation of the free hydroxyl groups present in native hemicelluloses could be achieved (Sun et al. 1999). The minimum amount of degradation of the hemicellulose chains was observed when this process was conducted.

Hemicelluloses esterified with fatty acids can find their applications in industries for coating paper/board. They exhibit unique hydrophobic and high moisture barrier properties. Oleoylation increases the hydrophobicity. Hence, the water resistance of the esterified hemicellulose is significantly higher than the water resistance of the acetylated hemicellulose when the degrees of substitution are the same. The use of esterified hemicellulose is preferred over the use of acetylated hemicellulose to develop barrier films used for the production of packaging materials in the food industry.

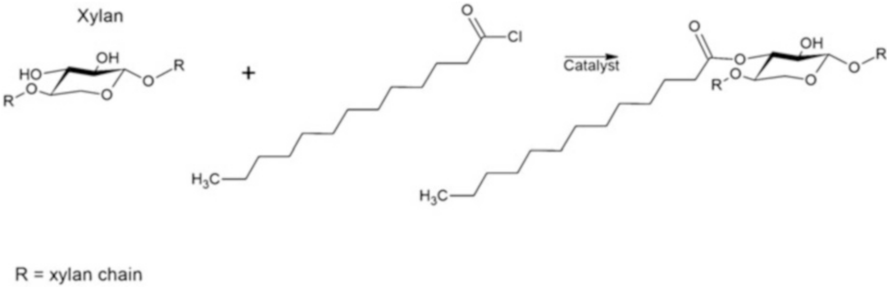


**Fig. 6.10** Reaction representing lauroylation of hemicellulose

### 6.3.1.3 Lauroylation

The lauroylation reaction is used to introduce lauroyl groups into the hemicellulose chains (Fig. 6.10). This reaction is generally carried out in the presence of a base and a catalyst (Fang et al. 1999). Lauroyl chloride is a common lauroylation agent. It can be efficiently used to esterify hemicellulose (Wang et al. 2012; Xu et al. 2008; Ren et al. 2008b).

Lauroylation resulted in increased hydrophobicity and decreased thermal stability (Wang et al. 2012; Xu et al. 2008). Lauroylated hemicellulose exhibits a regular and homogenous morphology. The homogeneity increases as the amount of the lauroylating agent increases (Wang et al. 2012).

The degrees of substitution were in the range of 0.43–1.82 when ILs were used as the reaction (lauroylation) solvents. A significant amount of the hemicellulose polymers could be degraded in the IL media under harsh reaction condition. The extent of degradation increased as the reaction time and reaction temperature increased (temperature: increased till 100 °C, reaction time increased till 90 min) (Wang et al. 2012). The thermal stability of the lauroylated hemicellulose (with a low degree of substitution) was lower than that of the native hemicellulose. The thermal stability of the lauroylated polymer (with high degrees of substitution) was higher than that of the unmodified hemicellulose (Wang et al. 2012; Xu et al. 2008; Ren et al. 2008b).

The lauroylation conditions were investigated. The effects of using various catalysts such as 4-dimethylaminopyridine, *N*-bromosuccinimide, *N*-methylpyrrolidine, *N*-methylpyrrolidinone, and pyridine were tested (Peng et al. 2008). The reaction rate was accelerated when the catalyst concentration was 5% (w/w, dried hemicelluloses). This resulted in increased product yield (from 56.2% (control sample) to 83.2%) and degree of substitution (from 0.82 (control sample) to 1.54) in the absence of a catalyst. The maximum reaction rate was obtained when the concentration of 4-dimethylaminopyridine was 5% (w/w, dried hemicelluloses). The lauroylation yield was 83.2% and the degree of substitution was 1.54. An increase in the concentration of 4-dimethylaminopyridine resulted in a decrease in the efficiency. However, the cost-inefficiency of the method limits the industrial use of such catalysts. The recovery of the catalyst is economically unviable (Peng et al. 2008).

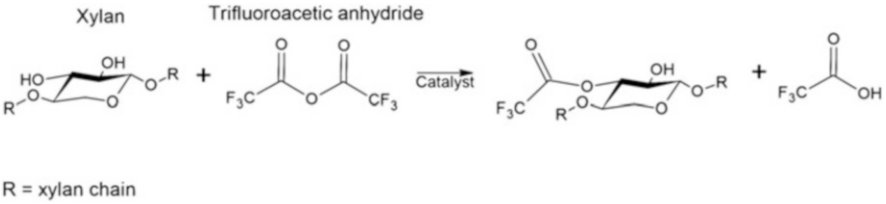


**Fig. 6.11** Fluorination of hemicellulose with trifluoroacetic anhydride

#### 6.3.1.4 Fluorination

Fluorine molecules are introduced into the hemicellulose chains following the process of fluorination (Fig. 6.11). Polymers with unique chemical and surface properties are produced post fluorination. Super-hydrophobic fluorinated polymeric materials have been reported. These materials exhibit good chemical resistance and stability. A strong barrier toward gases and liquids is formed and a low coefficient of friction is recorded (Tressaud et al. 2007; Woodward et al. 2003). These characteristics make the fluorinated polymers suitable candidates for the preparation of marine coatings, medical implants, plasticized films, and protective clothing (Woodward et al. 2003).

A common method of fluorinating hemicellulose is to carry out the fluorination reaction in a fluorine containing atmosphere. This method can be used to synthesize a wide variety of fluorine-based compounds with altered surface properties (Tressaud et al. 2007). The various fluorinated gases used for fluorination are $CF_4$, $CHF_3$, $C_3F_8$, $C_4F_8$, $NF_3$, $SF_6$, $F_2$, $NF_3$, $ClF_3$, and $C_4F_6O_3$ (Cardinaud and Tressaud 2000; Tressaud et al. 2007; Gröndahl et al. 2006). The elementary stages are highly exothermic and fluorination proceeds spontaneously at room temperature. This process can find its utility in industries (Tressaud et al. 2007).

The process of fluorination can be potentially used to modify the surface of arabinoxylan films. This results in reduced hydrophilicity. The contact angle increased from 30° (indicating hydrophilicity) to 70° for an arabinoxylan film containing 7% fluorine. The moisture content decreased from 18% to 12% (Gröndahl et al. 2006).

#### 6.3.1.5 Crosslinking/Graft Copolymerization

Crosslinking reactions can be used to esterify polymers (Fig. 6.12). The modified polymers resist thermal degradation and exhibit decreased solubility. This results in improved water resistance properties (Shao et al. 2019). The polymers are also resistant to creep and cold flow (Goodman 1999). Copolymerization applied to hemicellulose used in film formation improves the resistance to cracking by liquids and other harsh environments (Zhao et al. 2020).

Crosslinked hemicellulose is primarily used to produce hydrogels that exhibit limited water solubility and the ability to swell in water (Peng et al. 2011). Hydrogels are three-dimensional, hydrophilic, polymeric networks capable of imbibing large amounts of water or biological fluid into them. Different functional groups can be

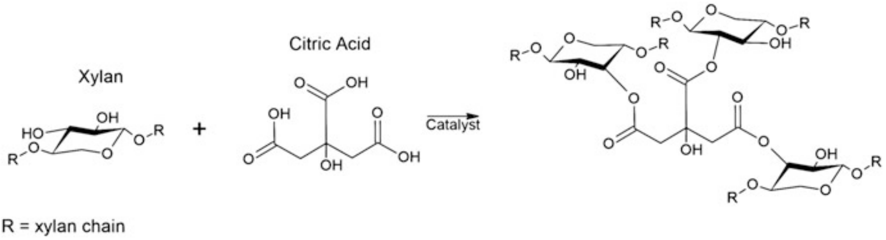


**Fig. 6.12** Crosslinking reaction with hemicellulose and citric acid

easily incorporated into the physically or chemically crosslinked networks to produce novel hydrogels. An increase in the degree of crosslinking results in a decrease in the distance between the crosslinking points. The volume of the available space for water absorption decreased. The hydrophobicity is increased as less amounts of free water are retained in the network.

At elevated temperatures and in the presence of catalysts such as sodium hypophosphite, carboxylic acid groups form five-membered cyclic anhydrides in the first stage. These further react with the hydroxyls groups present in the carbohydrate to form ester linkages (Xiaohong and Yang 2000; Mao and Yang 2001). The abstraction of the hydrogen atom from the hydroxyl groups present in the hemicellulose backbone results in the generation of active centers on the hemicellulose backbone that initiate the radical polymerization reaction. A crosslinking reagent can be used to produce a copolymer network exhibiting a crosslinked structure (Peng et al. 2011).

The popular crosslinking agents used to crosslink different polysaccharide-based materials are formaldehyde-based reagents, *N*,*N*-methylenebisacrylamide, vinylethylbenzene, and ethyldiol methacrylate (Hernadi 1999). However, the formaldehyde-based crosslinking agents can negatively affect human health and the environment. The less toxic polycarboxylic acids such as oxalic acid, citric acid, maleic acid, succinic acid, itaconic acid, and butane tetracarboxylic acid, which can be used as crosslinking agents, have attracted immense attention.

The incorporation of citric acid into the hemicellulose scaffold resulted in a significant increase in the oxygen barrier and hydrophobicity of the films formed from such polymers. The maximum tensile strength was recorded when the citric acid content was 20%. A further increase in the citric acid content resulted in a decrease in the tensile strength (Shao et al. 2019).

Crosslinking reactions in the presence of dihydroxymethyl(propionic acid) resulted in the formation of hyperbranched hemicellulose. The number of carboxyl and hydroxyl groups increased and a polymer with an increased number of active end groups was produced, which can effectively adsorb different kinds of dye. The maximum degree of substitution recorded was 0.83, which increased the viscosity to an appropriate dye adsorbing value. The produced polymers can efficiently adsorb dyes. The adsorption yields were recorded to be 825 mg/g for methyl red, 675 mg/g for bromomethyl green, and 912 mg/g for bromophenol blue (Zhang et al. 2019).

## 6.3.2 Etherification of Hemicellulose

Alcohol reacts with an alkylating agent in the presence of a base to form an ether bond (etherification reaction; Fig. 6.13). The alkylating agents that can be used in the reactions are alkyl halides (chlorides, bromides, and iodides), alkyl sulfonates, vinyl monomers, and epoxides. An epoxide is an unstable 3-member ring compound containing an oxygen atom in the ring that induces electron withdrawal from the adjacent carbon atoms (Shao et al. 2020). This increases the reactivity of the epoxide and they can efficiently react with alcohol-containing molecules such as hemicellulose.

The hemicellulose can potentially degrade in the presence of a base. A decrease in the degree of polymerization was recorded when the reaction was carried out in the presence of a base. The use of a base also resulted in the formation of compounds exhibiting poor mechanical properties (Ibn Yaich et al. 2017). Therefore, it is possible to obtain etherified hemicellulose by directly precipitating alcohols (Shao et al. 2020).

Etherification of polysaccharides can help tune the solubilities of the compounds. Etherification imparts stability to the molecules against microorganisms (biodegradability). These compounds exhibit film-forming abilities and increased viscosities (Shao et al. 2020). Etherified hemicellulose can be used to form films with enhanced mechanical properties such as hydrophobicity, thickness, tensile strength, and thermal stability (Shao et al. 2020).

The ether bond is more stable than the ester bond. The ester bond can be easily hydrolyzed (especially under alkaline conditions) (Pourchez et al. 2006). Methylation (Petzold et al. 2008; Fang 2002), alkylation (Shao et al. 2020), carboxymethylation (Alekhina et al. 2014; Petzold et al. 2006; Ren et al. 2008a), and benzylation (Junli et al. 2012; Hartman et al. 2006) are a few types of etherification reactions.

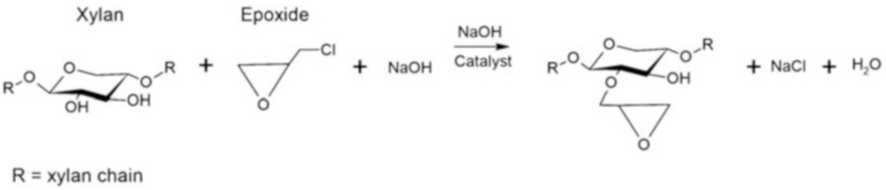


**Fig. 6.13** Etherification of hemicellulose in the presence of epoxide under alkaline conditions

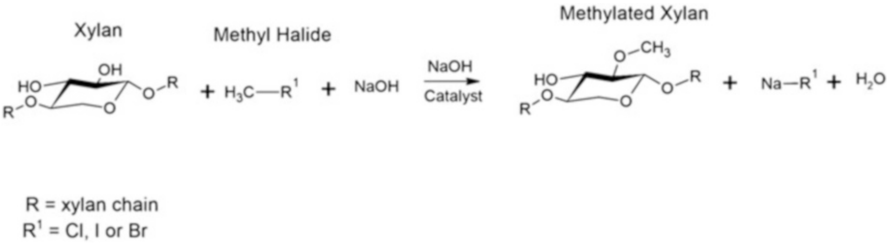


**Fig. 6.14** Reaction representing the methylation of hemicellulose

#### 6.3.2.1 Methylation

Methylation reactions are used to introduce methyl groups into the hemicellulose chain. Etherification reactions can be carried out for methylating compounds. Methyl halides such as methyl chloride and methyl iodide are used as the reagents (Fig. 6.14). The accessibility of the functional groups and the probability of the reaction between the functional groups of the reagents are increased when the hemicelluloses are activated. Heterogeneous activation of the material can be achieved. The dissolved polymer can be used as the starting material (Petzold et al. 2008) and sodium hydride (or sodium hydroxide) is used as the activator (Petzold et al. 2008; Fang 2002).

Factors such as the degree and uniformity of substitution, degree of polymerization, and molecular weight distribution influence the chemical and physical properties of the derivatives. Water-soluble products that exhibit a certain degree of amphiphilicity can be produced by methylating the compounds (Petzold et al. 2008).

Methyl xylan was synthesized using methyl chloride (or methyl iodide) as the etherifying agent. Xylan was reacted with an excess of methyl chloride (under pressurized conditions) in the presence of aqueous NaOH (40%) to yield methyl xylan (degree of substitution: 0.94) (Petzold et al. 2008). The strongly basic methylsulfinyl carbanion was used to generate the methylated hemicellulose ether. Hemicellulose obtained from wheat straw was used as the substrate. Methyl iodide and sodium hydride were used as the etherification agent and catalyst, respectively. The degree of substitution was 1.7. The thermal stability of the product increased upon methylation. The process can potentially lead to the degradation of hemicellulose (Fang 2002).

Methylation reactions resulted in the derivatization and fractionation of the sawdust. The methylation reaction was carried out in dimethyl sulfoxide/tetrabutylammonium to yield methylated cellulose, hemicellulose, and lignin. Methylated hemicellulose exhibited amphiphilic properties and could be used as a surfactant. These compounds possessed a flexible backbone. The hydrophilicity of the compound can be attributed to the presence of a relatively short molecular chain (Miki et al. 2020).

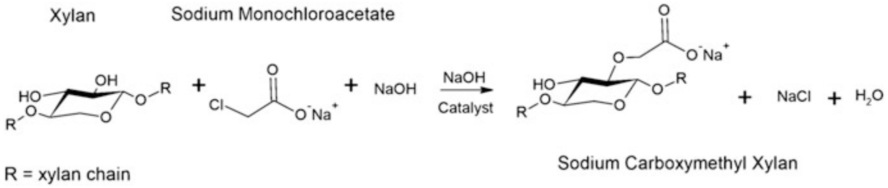


**Fig. 6.15** Carboxymethylation of hemicellulose using sodium monochloroacetate

### 6.3.2.2 Carboxymethylation

Carboxymethylation is a process following which carboxymethyl groups are introduced into the hemicellulose chain. Etherification reactions can be conducted to introduce the carboxymethyl groups. Etherification agents (such as sodium monochloroacetate; Fig. 6.15) (Petzold et al. 2006) are used during the process. It is a versatile functionalization process that provides access to bio-based materials that exhibit interesting properties. These materials can be used for inspissation, filming, emulsification, producing suspensions, maintaining water quality, and binding target molecules (Heinze 1998; Geng et al. 2020).

The carboxymethylation reaction can proceed in a suspension containing hemicellulose and ethanol/water. The reactions can be carried out under alkaline conditions. Under these conditions, the hemicellulose is activated. However, a substantial amount of the hemicellulose polymers can degrade during the carboxymethylation reaction carried out under alkaline conditions.

The hemicelluloses isolated from sugarcane bagasse were effectively converted into carboxymethylated hemicellulose compounds in the presence of sodium monochloroacetate and sodium hydroxide. A solution containing ethanol and water was used as the reaction medium. The maximum degree of substitution was 0.56. A significant amount of the polymers degraded during the process. The thermal stability of the compounds increased (Ren et al. 2008a). Reaction conditions used to carboxymethylate xylan were followed. Sodium monochloroacetate and sodium hydroxide were used as the reagents and 2-propanol was used as the reaction medium. Under these conditions, the degree of substitution was found to be 1.22 (Petzold et al. 2006).

An increase in the water absorption ability (at high relative humidity) was observed during the xylan carboxymethylation process that resulted in the production of bioplastic. This indicated that the carboxymethyl groups were hydrophilic in nature. The hydrophilicity promotes biological and abiotic degradation (Alekhina et al. 2014). Carboxymethylation of hemicellulose (obtained from poplar) was conducted using sodium chloroacetate and sodium hydroxide as catalysts. A solvent system consisting of ethanol and water (ethanol/water; 80% (v/v)) was used as the reaction solvent. The degree of substitution was found to be 0.61 when the reaction was carried out for 60 min at a temperature of 85 °C. Peeling occurred at high temperatures in the presence of sodium hydroxide, resulting in the slight degradation of hemicellulose. Films formed from carboxymethylated hemicellulose exhibited increased hydrophilicity, water vapor permeability, and elongation at break values. The tensile strength and oxygen permeability decreased (Geng et al. 2020).

The degree of substitution was recorded to be 0.45 when hemicellulose was carboxymethylated at 70 °C. The reaction was allowed to proceed for 2 h in a solvent system consisting of isopropanol and water (isopropanol:water = 25:75, v/v). Potassium hydroxide (KOH) supported on natural zeolite clinoptilolite (CP) was used as the catalyst. The reaction was carried out under varying KOH: CP ratios and the optimum ratio was found to be 1:2. The efficiency of the reaction, when the optimized catalyst concentration was used for the reaction, was approximate twice the efficiency of the reaction carried out using standard KOH solution (even under conditions of shorter reaction time and lower temperature). Under the optimized conditions, less amounts of hemicellulose were degraded (Khalilzadeh et al. 2019).

Carboxymethylated beechwood xylan was produced under alkaline conditions when sodium chloroacetate was used. The influence of the process parameters on the degree of substitution of xylan was explored. Carboxymethylated xylan with degree of substitution of 0.21 was produced under the optimized conditions (NaOH 0.75 M; reaction time: 2 h; 70 °C). The process of carboxymethylation resulted in increased molecular weight and enhanced thermal stability (Konduri and Fatehi 2016).

### 6.3.2.3 Benzylation

Benzylation of hemicellulose involves the introduction of benzyl groups into the hemicellulose scaffold. The hydrogen atoms present in the hydroxyl groups in hemicellulose chains are replaced by the benzyl groups present in benzylating agents such as benzyl chloride (Fig. 6.16) (Sereshti and Mohammadi-Rovshandeh 2003). During the process, the natural fibers are pre-swelled for 1 h using concentrated sodium hydroxide. Following this, they are reacted with benzyl chloride in the presence of a phase transfer catalyst. The reported reaction was carried out at 120 °C and the reaction time was varied between 5 and 10 h. Subsequently, the benzylated fibers were washed with water and dried under vacuum at 80 °C (Patel and Parsania 2018).

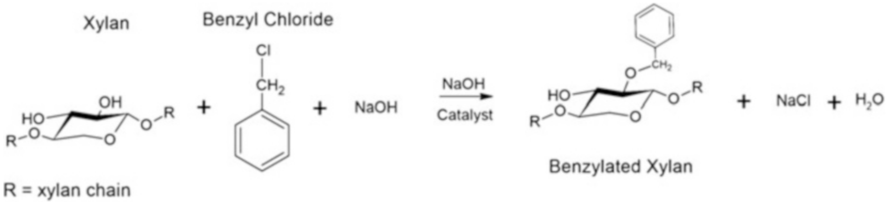


**Fig. 6.16** Reaction representing the benzylation of hemicellulose in the presence of benzyl chloride

Etherification (benzylation) resulted in increased thermal stability and hydrophobicity as benzene ring was introduced into the hemicellulose chain. The benzylated hemicellulose can be potentially used for the production of hydrophobic films that can be used for packaging food items. These films can also be used to coat surfaces (Talja et al. 2010).

Hydrophobic hemicelluloses with increased thermal stability were formed when hemicelluloses obtained from wheat straw were benzylated using benzyl chloride in the presence of sodium hydroxide as the catalyst. The reaction was carried out in an ethanol/water system (Junli et al. 2012). The process of benzylation helped develop oxygen barrier films. Hemicellulose present in wheat straw was used as the substrate. The films exhibited high hydrophobicity and were moisture-resistant (Hartman et al. 2006).

## 6.4 Concluding Remarks

Hemicelluloses can find their applications in various industrial fields. Hence, polysaccharides have been structurally modified to improve various properties such as hydrophobicity, thermal stability, viscosity, solubility (in different solvents), biocompatibility, and water resistance. The ability of the polysaccharides to resist degradability (in the presence of microorganisms) can also be improved. In the first step, hemicellulose is isolated from biomass. The choice of the solubilization/isolation method depends on the use of the obtained carbohydrates. The degree of polymerization varies as the solubilization method is varied. The type of substituents introduced into the hemicellulose chains, monomer released, and degradation products formed depend on the solubilization method. Hemicellulose for film formation can be produced following the method of alkaline solubilization. In this method, the bonds between hemicellulose and lignin units are broken, but the degree of polymerization is retained. The dilute acid pretreatment method can be used to yield products that can be used to produce bioenergy. The lignin structure is modified and sugar molecules are released as oligosaccharides or monosaccharides. These are subsequently fermented. The alkaline solubilization method can be potentially used to obtain fermentable sugars but it requires followed step of acid or enzymatic hydrolysis.

Hemicellulose can be chemically modified and used to produce bioplastic, paper coatings, medical implants, and hydrogels. Acetylation of hemicellulose is carried out to produce films/bioplastics. Acetylation results in increased hydrophobicity and enhanced thermal stability. The ability of hemicellulose to form strong hydrogen-bonded networks decreases post-acetylation. Hemicelluloses are crosslinked to produce hydrogels. Crosslinking results in increased resistance toward thermal degradation and decreased solubility. Carboxymethylation and benzylation (etherification methods) of hemicellulose are conducted to produce biodegradable hydrophobic materials. This method is also followed to produce amphiphilic hemicellulose derivatives (such as surfactants) that can be produced by methylating hemicellulose.

There is a worldwide demand to identify renewable energy sources. Hemicelluloses can be potentially used to generate energy and can find applications in various industries. They are environmentally friendly and will be predominantly used in various fields in the near future. The solubilization process is cost-ineffective, and corrosive or hazardous substances need to be used. Moreover, hemicellulose needs to be chemically modified to improve the properties of the final products. Research is being conducted with hemicellulose as it is a readily available material (found in agricultural residues) and can be used to address the problem of shortage of energy. The results can be used to expand the application prospects of hemicellulose.

**Acknowledgments** The authors thank the São Paulo Research Foundation (FAPESP grant number 2017/22401-8; 2019/12997-6) for financial support.

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# Enzymatic Approach on the Hemicellulose Chain Structural Modification and the Main Enzymes Production and Purification

# 7

Danilo Bueno, Caroline de Freitas, and Michel Brienzo

## Abstract

Hemicellulose, one of the main components of lignocellulosic biomass, has great potential as a raw material to produce high value-added bioproducts such as hemicellulose-based films/bioplastic and biomaterials. Xylan is the major hemicellulose in grasses, and the second most abundant polysaccharide found in nature, corresponding to approximately one-third of the planet's renewable carbon source. Xylan bioplastic can respond to external stimuli, such as pH, temperature, ionic strength, among others. For this reason, these films/bioplastics are highlighted because of their wide industrial utility as an oxygen barrier in packaging, an adhesive or additive in plastics, food additive, and stabilizer, a hydrogel in medical applications such as artificial skin and drug encapsulation. However, to improve its applicability and versatility, the molecular structure of xylans can be modified by the action of accessory enzymes such as *α-glucuronidase* and *α-L-arabinofuranosidase*. These enzymes hydrolyze pending groups in the xylan chain, decreasing their solubility and helping in the formation of aggregates, also increasing its adsorption in relation to cellulosic substrates. Structural modification can be performed by esterification, stearation, acylation, and oxidation, resulting in xylan derivative with specific properties. This chapter showed possible changes in the xylan structure through the application of enzymes for properties improvement.

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M. Brienzo (ed.), *Hemicellulose Biorefinery: A Sustainable Solution for Value Addition to Bio-Based Products and Bioenergy*, Clean Energy Production Technologies, https://doi.org/10.1007/978-981-16-3682-0_7

**Keywords**

Xylan · Xylanase · Esterification · Stearation · Acylation · Oxidation

## 7.1 Introduction

Biomass is composed basically of cellulose, hemicellulose, and lignin. There are many examples of biomass types around the world, such as softwood, hardwood, grasses, food waste, among others. Worldwide, energy is produced mainly from non-renewable sources such as oil and coal, which makes lignocellulosic biomass an important renewable source for bioenergy production. Moreover, bioproducts from polymers (biopolymers) represent a feedstock source for value-added products. However, lignocellulosic biomass represents a raw material source little exploited in industrial-scale biotechnological processes. Therefore, researches about new applications are emerging and can provide a better use of these materials. In this context, it is known that besides the importance in biofuel production, biomass hemicelluloses can still be used to obtain various products of industrial interest, such as bioactive compounds, furfural, hydrophilic acid, bioplastic/biomaterials among others (Freitas et al. 2021; Abe et al. 2021a; Abe et al. 2021b; Takkellapati et al. 2018). In addition to sugarcane biomass, which is the main raw material for biofuels production in Brazil, several other biomasses such as corn/stalk cob, soybean/stems, rice straw, wheat straw, cotton, and coffee, have potential use in obtaining biofuels and high value-added products. Another important waste, in tropical countries, is fruit waste where Brazil stand out with the production of fruits banana, guava, and orange (Pereira et al. 2021).

For each ton of sugarcane processed for juice extraction, 140 kg (dry basis) of bagasse are generated (Fernandes et al. 2020). It is estimated that for the 2020/2021 sugarcane harvest in Brazil, there will be a total production of 665,105 million tons of sugarcane, which is about 3.5% higher than the previous harvest (2019/2020) (Aguiar 2021). In the southeast region of Brazil, around 420.71 million tons of sugarcane are produced. From this amount, it is estimated a production of 93,115 ton of bagasse, which has available around 23,278 ton of hemicellulose.

Hemicellulose is widely available considering sources such as agro and industrial wastes (Melati et al. 2017). Hemicellulose can be a raw material for several industrial products via biotechnological and chemical routes. Based on the importance of this polysaccharide and its products, this chapter aims to describe the enzymatic structural modifications of hemicellulose to obtain products with high value-added. The production and purification of the main enzymes (xylanases) responsible for chain modification were presented.

## 7.2 Hemicellulose and Other Components in Biomass

The morphological characteristics attributed to cell wall components of the lignocellulosic biomass are responsible for the difficulty in using them as raw material. Naturally, lignocellulosic materials are resistant to enzymatic or microbial degradation, which occurs due to the organization of the components, where cellulose is embedded in a matrix composed of hemicellulose and lignin. Hemicellulose is chemically linked to lignin (Zamora et al. 2020), while its association with cellulose occurs through physical interactions in the fiber surface, presenting chains between cellulose fibers.

Cellulose is the main constituent of the plant cell wall. Cellulose is composed of a linear chain of 7000 to 15,000 glucose residues joined by β-(1,4) glycosidic bonds, without branches. The β-type bond causes a rotation (180°) alternating the glucose unit. This rotation provokes a linear chain structure (Fengel and Wegener 1984). Lignin is another molecule that appears together with cellulose and lignin in the plant cell wall. The lignin collaborates with the resistance and recalcitrance of the lignocellulosic material.

Lignin is a macromolecule composed of phenylpropane units: guaiacyl (G), syringyl (S), and *p*-hydroxyphenyl (H) units. The coupling of the phenylpropane units does not occur in a regular and repetitive way, due to the biosynthesis mechanism, which is processed via the radical from the reaction of three precursor cinnamic alcohols, forming a three-dimensional and amorphous macromolecule (Schmatz et al. 2020). Its composition varies between different groups of plants: in gymnosperms, type G (guaiacyl) predominates, in angiosperms, GS (guaiacyl-syringyl) and in grasses such as sugarcane bagasse, GSH-type lignin (guaiacyl) stands out (Higuchi 2006). Cellulose-hemicellulose-lignin complex presents recalcitrance that limits the enzymatic hydrolysis of cellulose and hemicellulose (Shimizu et al. 2021). Recalcitrance occurs since hemicellulose difficult access to cellulose, which presents rigidity and crystallinity, and lignin is the main recalcitrant component due to plant defense and prevention to phytopathogens and their hydrolytic enzymes (Houfani et al. 2020).

Hemicelluloses, in general, consist of 80 to 200 units of sugar residues, of which pentoses (D-xylose, L-arabinose, and L-rhamnose), hexoses (D-glucose, D-mannose, and D-galactose), and uronic acids (4-*O*-methyl-D-glucuronic and D-galacturonic acids) (Xu et al. 2013; Fengel and Wegener 1984) (Fig. 7.1). The hemicellulose chain can consist of a single monosaccharide (xylans) or two or more units (xyloglucans, 4-*O*-methyl-glucuronoxylan) (Fig. 7.2). Despite presenting an amorphous structure, hemicellulose is capable of forming hydrogen bonds and tends to crystallize after removing the side chains. The substituting groups, arabinosil and acetyl, decrease the adsorption of hemicellulose to cellulose (Kabel et al. 2007). This change in the pending group interferes with the properties and is the key in hemicellulose biological modification to improve its application.

Over the years, assessments have been made regarding the property of hemicellulose in forming films when combined with small concentrations of chitosan (5–10%). It has been reported that the addition of these levels of chitosan to

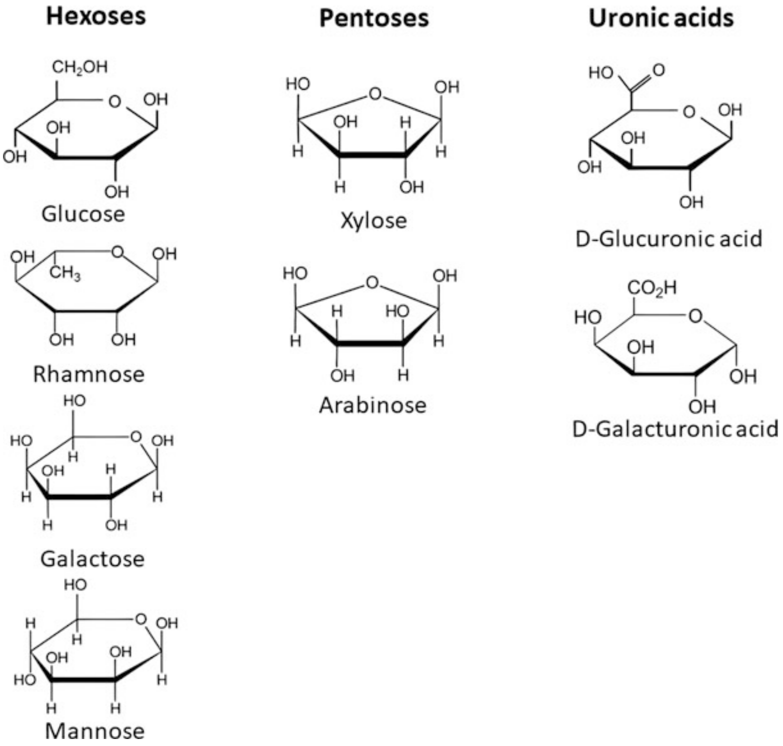

**Fig. 7.1** Structure of hemicellulose main components

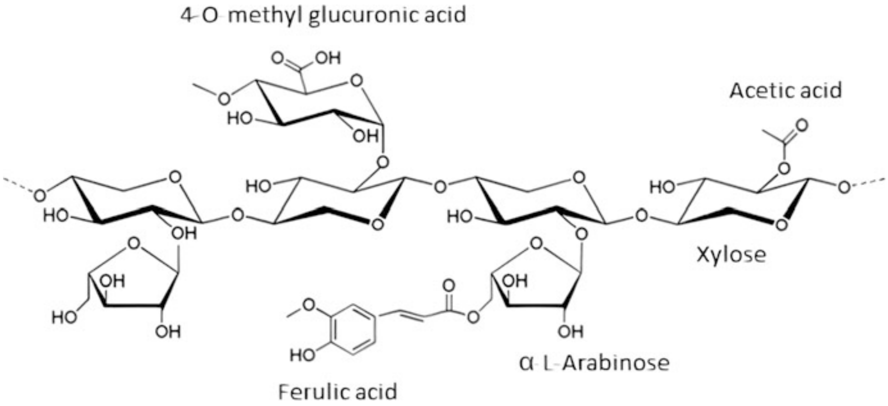

**Fig. 7.2** Xylan structure

hemicellulose increases the crystallinity of the film due to interactions between xylan acid groups and chitosan amino groups (Gabrieli et al. 2000).

Xylan is the hemicellulose present in a greater proportion in the sugarcane bagasse, around 25% (Melati et al. 2021; Alves et al. 2020; Brienzo et al. 2016). In the industry, the use of xylan to obtain bioproducts has gained prominence through the manufacture of packaging, hydrogels, production of ethanol and lactic acid through the fermentation of xylan monomeric sugars by microorganisms, and additionally, furfural production by xylan hydrolysis and dehydration of xylose monomers, and finally, obtaining xylitol via xylose hydrogenation pathways (Abe et al. 2021a; Naidu et al. 2018).

Hemicellulose can be obtained through chemical, physical, physicochemical (Melati et al. 2017), and biological and chemical pretreatment combined (Felipuci et al. 2021) from different sources, such as sugarcane bagasse and straw, softwoods and hardwoods, soybean, algae, macaúba, babaçu, buriti, sunflower, spent coffee ground, elephant grass and sorghum (Martins et al. 2021; Shimizu et al. 2020; Santos et al. 2018; Chiyanzu et al. 2014), among others. Xylan is the main type of hemicellulose and is also the most abundant biopolymer found in these agroindustrial wastes (Martins et al. 2021; Urtiga et al. 2020; Melati et al. 2019).

## 7.3 Hemicellulose Bioproducts

Hemicellulose is a raw material for several industrial products such as xylooligosaccharides (XOS), xylitol, hydrogel, dressings, and substitutes for human skin, films for biodegradable packaging, drug encapsulation, substitute for fat in cheeses, additives in paper production, substitute for gelatin in food gums, additives in the textile and cosmetics industry (Freitas et al. 2019; Ebringerová 2006). Hemicellulose is constantly focusing on the study with the aim of improving its applications, such as XOS with high purity (Forsan et al. 2021; Freitas et al. 2019; Reddy and Krishnan, 2016), films (Hanif and Zaman 2017), xylan-based thermoplastic (lactate copolymer) (Zhang et al. 2017), and also for biomedical applications (Cantu-Jungles et al. 2017). Among the high value-added bioproducts obtained from hemicellulose, hydrogel, a product with high added value due to its properties, stands out. Hydrogels have the ability to respond to external stimuli, such as pH, temperature, ionic strength, etc. (Qiu and Park 2001). In the literature, hydrogels are defined as 3D polymer networks with a high degree of flexibility and high capacity of retaining water or biological fluids (Ullah et al. 2015).

Since first reports in the literature about hemicellulose films (Smart and Whistler 1949), hemicellulose-based hydrogels have gained prominence for their wide industrial utility, as a biological skeleton for tissue engineering, a biosensor, as barriers for the regulation of biological adhesions, and it can also be used in the encapsulation of living cells and drugs (Sun et al. 2013). In the literature, there are reports of many xylan-based hydrogels obtained by conversion of different biomasses, such as corn cob xylan, oat spelt xylan, rye xylan, aspen wood xylan, corn hull xylan, barley husk xylan, cotton stalk xylan, birchwood xylan, and beechwood xylan (Urtiga et al. 2020). These products have different physicochemical properties since hemicellulose from which the biofilms were obtained are a heterogeneous macromolecule.

Hemicellulose modification is desirable for film and biomaterial improvement. There are different approaches in the search for better conditions of resistance, elasticity, and hydrophobicity of the film, such as (I) additions of plasticizer agents such as xylitol and glycerol to the hemicellulose film (Gröndahl et al. 2004); (II) mixtures of natural polymers to the film, such as starch (Zhang and Whistler 2004); (III) chemical modifications of hemicellulose film by introducing pendent groups to main chain (esterification, etherification, acetylation, among others).

Hemicellulose presents a wider potential in industrial applications. In this context, hemicellulases have a key factor in hemicellulose conversion to high added value products, both xylanases, and β-xylosidase that hydrolyze xylan main chain and accessories enzymes that hydrolyze xylan pendent groups, described in more details in the next topic.

## 7.4 Enzymatic Modifications of Xylan

Xylan application can be empowered by modification of its chain, and as result improve its properties. Structural modifications of the xylan chain can be done by enzymatic action. Enzymes can hydrolyze xylan into oligosaccharides and monosaccharides, important carbohydrates in the biotechnology industry. Endo-β-1,4-ᴅ-xylanase (EC 3.2.1.8) acts on the xylan backbone and generates a low degree of polymerization chain, the xylooligosaccharides. XOS are substrates for β-xylosidase, which acts through the non-reducing terminal releasing ᴅ-xylose (Freitas et al. 2019). These enzymes are responsible for the modification of the main chain, and in addition there are enzymes that hydrolyze the pendant/side groups. The enzymes responsible for the hydrolysis of side groups are defined as accessory enzymes. Once the accessory enzymes release the side groups, the xylanases can efficiently act on the xylan backbone. Arabinose side groups are removed by the action of α-ʟ-arabinofuranosidase (EC 3.2.1.55), α-glucuronidase (EC 3.2.1.131) removes glucuronic acids, and acetyl-xylan esterase (EC 3.1.1.72) removes the acetyl groups (Juhász et al. 2005). Ester bonds between hydroxycinnamic acids

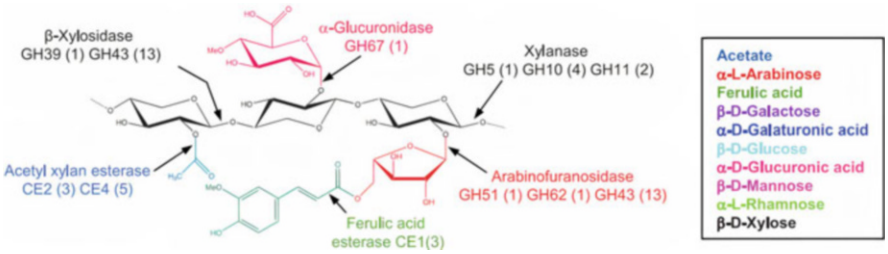

**Fig. 7.3** Xylan hydrolysis with xylanases and accessories enzymes (Deboy et al. 2008)

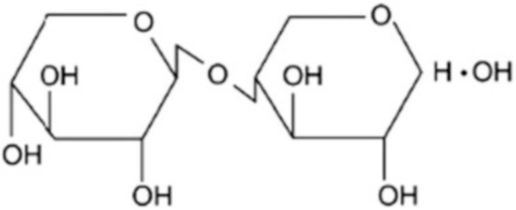

**Fig. 7.4** Basic xylooligosaccharides (XOS) structure

and sugars are breakdown by the action of feruloyl esterase (Malgas et al. 2019; DeBoy et al. 2008) (Fig. 7.3). The accessory enzyme action can produce a debranched xylan, which means no side groups are attached. This debranched xylan chain can be from interest of biomaterial production as well as for xylooligosaccharides that will not present side groups.

The α-glucuronidases are classified into two families, the GH 67 and GH 115. The GH 67 α-glucuronidases cleaves uronic acids linked to the non-reducing terminal of xylosil residues of small xylooligosaccharides. The GH 115 α-glucuronidases hydrolyzes 4-*O*-D-methylglucuronic acids linked to non-reducing terminals xylopropanosyl residues and those linked to internal xylosyl residues. Bacteria and fungi are known as producers of the α-glucuronidase families GH 67 (about 70 kDa) and GH 115 (about 90 kDa), respectively (Yeoman et al. 2010; Dimaragona and Topakas 2016).

Both bacteria and fungi produce the accessory enzyme acetyl-xylan esterases. Acetyl groups from heteroxylans are cleaved by the action of the acetyl-xylan esterases. The microorganisms producing these enzymes are capable of degrading acetylated xylans. Feruloyl esterases cleave bonds between esterified hydroxycinnamic acids in arabinoxylans. This enzyme is produced by both fungi and bacteria, with an important role in lignocellulosic material decay. Feruloyl esterase production can be induced according to the presence of certain substrates in microbial medium growth (Komiya et al. 2017; Hettiarachchi et al. 2019).

Debranched xylan, without side groups, is an important bioproduct in industrial applications such as xylooligosaccharides (XOS) (Linares-Pasten et al. 2018), sugar oligomers made with xylose units that have great prebiotic potential and nutrient benefits, promoting the growth of probiotic bacteria in the intestinal tract (Freitas et al. 2019). XOS are naturally present in foods, such as fruits and vegetables, however, they can be obtained by acid or enzymatic hydrolysis of xylan (Forsan et al. 2021; Brienzo et al. 2016) (Fig. 7.4). In addition to prebiotic effects on humans, XOS contribute to human health in the reduction of cardiovascular symptoms, alleviation of dental decaying, activation of calcium absorption, and also on bowel function improvement (Grootaert et al. 2007).

The XOS produced can vary in degree of polymerization and amount of monomeric units (Freitas et al. 2021; Freitas et al. 2019), taking into account that there are different sources of xylan with different chemical compositions due to the varied resources of lignocellulosic biomass. Since xylan's accessory enzymes can hydrolyze their pending groups (DeBoy et al. 2008), it is known that it is possible to obtain branched XOS or not, therefore, accessory enzymes play a key role in the production of XOS.

There are many reports in the literature of obtaining XOS via enzymatic hydrolysis with different xylanases from bacteria and fungi. A xylanase from *Bacillus halodurans* S7 (XynA) was applied to obtain XOS from wheat straw xylan (Faryar et al. 2015). Using the bacteria *Clostridium thermocellum* ATCC 27405 xylanase (XynZ), it was possible to obtain XOS from sugarcane xylan (Mandelli et al. 2014).

Besides bacteria, fungi also produce xylanases important for obtaining XOS. The fungus *Penicillium funiculosum* produces xylanase (XynD) that was used to obtain XOS from wheat xylan (Lafond et al. 2011). Another example, *Thermomyces lanuginosus* (IMI 84400, and IMI 96213) and *Erwinia chrysanthemi* produced the xylanses XynA (GH11 family) and XynA (GH30 family), and were successively used to obtain XOS from hydrolysis of beechwood glucuronoxylan (Puchart and Biely 2008).

Recently, literature reports about the development of enzyme mixtures, known as enzymatic cocktails, obtained from microorganisms, for XOS production, is increasing. In these studies, there is a debranching of xylan obtained through different biomasses by chemical pretreatment processes followed by enzymatic hydrolysis to obtain XOS (Reddy and Krishnan 2016; Costa et al. 2018). The composition and structure of XOS depend on the biomass used as raw material and also on the production processes. Obtaining XOS by the action of accessory enzymes, which hydrolyze the pending groups of xylan, is an attractive process due to the non-production of byproducts, since the action of such enzymes is specific for each pending group, as shown previously (Costa et al. 2018).

Auxiliary enzymes are important in obtaining several products with high added value. The *α-L-arabinofuranosidase*, for example, is an accessory enzyme that hydrolysis the pendent groups α-L-arabinose from xylan structure, being produced by both fungi and bacteria groups (Poria et al. 2020). This enzyme has wide industrial applications, such as increase digestibility in animal feed industries (Cozannet et al. 2017), enhance bread quality and texture (Zhou et al. 2019) in the food industry, increase reducing sugar content (Chadha et al. 2017) in biofuel industries, increase pulp delignification (Numan and Bhosle 2005).

The feruloyl esterase is another accessory enzyme, which hydrolysis ferulic acid pendent groups from xylan. This enzyme, for example, has a great potential in several industrial areas, such as chemical, animal feed, pulp and paper, food and agriculture, and also pharmaceutical industries due to the production of ferulic acid. In pulp and paper industries, feruloyl esterase has a key function by removing substitutions and linkages between polymers during pulping (Fazary and Ju 2008).

The α-glucuronidase is an accessory enzyme that hydrolysis xylan glucuronic acid pendent groups (Brienzo et al. 2008). This enzyme has been used with a mix of enzymes (glucooligosaccharide oxidase) to produce an important acid for industrial application, called 4-*O*-methyl-D-glucaric acid, a dicarboxylic acid, that offers several applications in detergent builder and biopolymer fields (Vuong and Master 2020).

**Table 7.1** Commercial xylanases based products and their industrial applications

| Product name | Company | Industrial application |
|---|---|---|
| Albazyme-10[a] | Ciba Giegy, Swiss | Food |
| Bacterial Xylanase XBK BX9 | Leveking, China | Bakery |
| Belfeed B1100 | Agrimex, Belgium | Food additives |
| Cartazyme | Clariant, UK | Pulp bleaching |
| Ecopulp | Alko Rajamaki, Finland | Pulp bleaching |
| Ecozyme | Thomas Swan, UK | Pulp bleaching |
| Luminase | Verenium, USA | Pulp bleaching |
| Nutri Xylanase Enzyme | Ultra Biologic Inc., USA | Food additives |
| Pulpzyme (HA, HB, HC) | Novo Nordisk, Denmark | Pulp bleaching |
| Sanzyme X | Sankyo, Japan | Food |
| VAI Xylanase | Voest Alpine, Austria | Pulp bleaching |

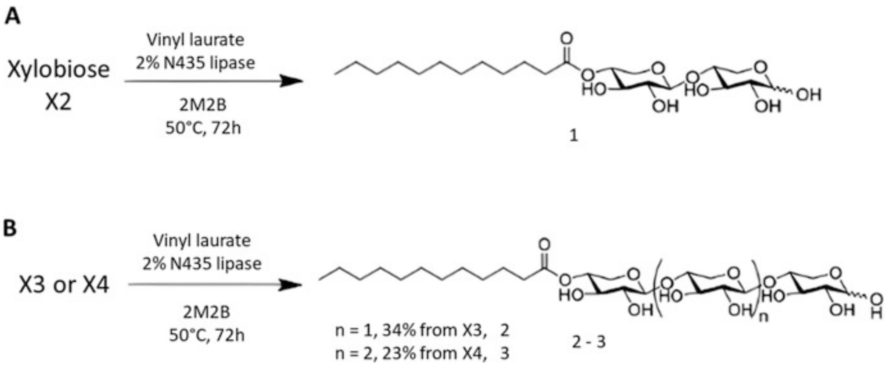

**Fig. 7.5** Fatty ester of xylooligosaccharides (Gérard et al. 2020). (**a**) Synthesis of 4′-*O*-laurylxylobiose 1 from xylobiose (X2). (**b**) Synthesis of 4″-*O*-laurylxylotriose 2 and 4‴-*O*-laurylxylotetraose 3 from xylotriose (X3) and Xylotetraose (X4), successively

Acetyl-xylan esterase is responsible for the deacetylation of xylan, that is, the removal of pending groups of acetic acid. Recently, this enzyme was applied to aspen xylan, and this application contributed to the reduction of recalcitrance and increased saccharification of this biomass (Wang et al. 2020), which for the fuel production sector are key factors in the process of obtaining biofuel.

Xylanases and accessory enzymes are produced and commercialized for different industrial applications. The mainly commercialized products are for the pulp and paper, and food industries (Chakdar et al. 2016; Goswami and Pathak 2013; Walia et al. 2017). These industrial products, producing company, and industrial application are summarized in Table 7.1.

Different from hydrolysis by xylanases and accessory enzymes, several other enzymatic modifications can be applied to the xylan chain, for example, xylan esterification. Fatty esters of XOS were produced from xylobiosis (X2), xylotriose (X3), and xylotetraose (X4) using a commercial lipase enzyme (Novozymes) as a catalyst in the presence of vinyl laurate (Gérard et al. 2020). It was obtained monoesters with no acyl chain at the OH-4 non-reducing terminal of xylose units (Fig. 7.5).

The commercial lipase Novozym 435 (*Candida antarctica*) (Novo Nordisk A/S) was applied as a catalyst in the formation of xylose caproate ester (Abdulmalek et al. 2016). The reaction was performed by xylose condensation, an aldopentose, and caproic acid in an organic solvent, showing high capacity and stability in esterification reactions. The study optimized the condensation of xylose and caproic acid in organic solvents (DMSO and acetone 1:10 (v/v)) using lipase as a catalyst in an incubation time of 24 h, at 60 °C and pH 10–11.

An increase in the superficial hydrophobicity of the films was observed with enzymatic modifications of xylan (Stepan et al. 2013). A combination of different commercial lipases (L1754 from *C. rugosa*, 86,012 from *R. oryzae*, L9031 from *Mucor miehei*, and L8906 from *M. javanicus*) (Sigma–Aldrich) with cutinases (Araújo et al. 2007) was used to promote acetylation with vinyl acetate and stearation with vinyl stearate in rye arabinoxylan films. The hydrophobicity of the surface increased with the acylation, what is desired for certain application such as resistance to humidity.

Xylan chain (grafted) was oxidized through enzymatic modifications (Pei et al. 2015). Oxidation of the xylan chain was promoted using phenols such as p-coumaric acid (PCA), ferulic acid (FA), syringaldehyde (SD), and vanillin (VA) in a reaction catalyzed by a commercial laccase (Novozymes). The reaction improved the molecular weight of xylan through these structural modifications using laccase, which led to better applicability of xylan when used as a film barrier. The film presented higher strength using xylan derivative and antibacterial effect to *Escherichia coli*, *Corynebacterium glutamicum,* and *Bacillus subtilis*.

In addition to xylans enzymatic modifications, esterification can be applied to polysaccharides in general, such as lignocellulose. Through esterifications, lignocellulose can be converted into high added value chemicals such as fatty acid esters (Siebenhaller et al. 2018). In this study, lipase B from *Candida antarctica* (Sigma-Aldrich) was used as a catalyst for the deep eutectic solvent (DES) reaction system for the sugar esterification with fatty acids. Through this approach, this study synthesized sugar esters based only on lignocellulosic biomass as raw material.

Several studies in the literature evaluate the use of lignocellulosic biomass as raw material for obtaining sugar esters via enzymatic esterification. A study similar to that of Siebenhaller et al. (2018) was prepared by Siebenhaller et al. (2017), in which it was possible to obtain glycolipids from glucose and xylose, previously generated by the acid pretreatment of lignocellulosic biomass. The glucose and xylose fractions were used to generate deep eutectic solvent (DES) in a reaction catalyzed by a lipase B (from *Candida antarctica*) (Sigma-Aldrich). Glycolipids are considered sustainable surfactants with great industrial potential.

## 7.5 Xylanases Production from Fungi and Bacteria

Xylanolitic enzyme production is induced by xylan presence in the growth medium, which most of the time it is the best inducer (Bueno et al. 2020; Calore et al. 2020; Fernández-Espinar et al. 1994). However, some studies demonstrated the inducing effect of fragments from xylan hydrolysis (Brienzo et al. 2012; Aro et al. 2005). Xylanase repression was demonstrated by the presence of readily assimilable sugars such as glucose, lactose, and xylose (Gaspar et al. 1997). Lignocellulosic materials (sugarcane bagasse, wood sawdust, etc.) can be used to obtain xylanolitic enzymes, with low substrate cost in submerged or solid culture (Nanjundaswami and Okeke 2020).

Several microbial species produce specific xylanases when growing in a medium containing xylan, with little or no cellulose production. However, cellulases are produced together with xylanases when microorganisms growing in a culture medium containing cellulose or cellulose-based material. One strategy used to obtain the cellulosic-free xylanolytic complex is the cultivation of microorganisms in a culture medium containing xylan not contaminated with cellulose (Bailey et al. 1992).

**Table 7.2** Microbial xylanases microorganism producers and properties

| Microorganism | Conditions | | Molecular weight (kDa) | Reference |
|---|---|---|---|---|
| | pH | Temperature (°C) | | |
| **Bacteria** | | | | |
| *Bacillus pumilus SSP 35* | 6 | 50 | 20 | Subramaniyan (2012) |
| *Bacillus halodurans* | 9 | 78 | 40 | Kumar and Satyanarayana (2013) |
| *Cellulosimicrobium cellulans CKMX1* | 8 | 60 | 58 | Walia et al. (2014) |
| *Paenibacillus macerans IIPSP3* | 4.5 | 60 | | Dheeran et al. (2012) |
| *Paenibacillus* sp. *NF1* | 6 | 60 | 37 | Zheng et al. (2014) |
| **Fungi** | | | | |
| *Aspergillus niger ANL-301 9* | 5.5 | 45 | 13.5–14 | Okafor et al. (2007) |
| *Geotrichum candidum* | 4 | 50 | 60–67 | Radionova et al. (2000) |
| *Trichoderma reesei* | 5 a 5.4,<br>4 a 4.5 | 45.4 | 20, 19 | Tenkanen et al. (1992) |
| *Penicillium capsulatum* | 5 a 5.5,<br>4 a 4.5 | 48 | 22 | Ryan et al. (2003) |
| *Penicillium* sp. *CGMCC 1669* | 3.8 | 40 | 21 | Liu et al. (2010) |

**Table 7.3** Industrial high value-added products obtained from xylose conversion and their applications

| Product | Industrial application | Reference |
|---|---|---|
| Ethanol | Biofuel | Matsushika et al. (2009) |
| Lactic acid | Food | Turner et al. (2015) |
| Xylonic acid | Dispersant | Raposo et al. (2017) |
| Succinic acid | Drug | Salvachuá et al. (2016) |
| Xylitol | Food | Rao et al. (2016) |
| Furfural | Solvent | Peleteiro et al. (2015) |
| Levulinic acid | Polymer precursor | Wang et al. (2018) |

Xylanolitic microorganisms are described in marine and terrestrial environments, including in extreme conditions such as hot springs, Antarctic environments, and saline lakes. Comparing bacterial and fungal xylanases, it is noted that bacterial xylanases belong to the GH10 family, whereas fungal xylanases belong to the GH11 family. In addition to the classification, the biochemical properties of endoxylanases produced from bacteria and fungi can vary. Among the main biochemical properties are molecule size (8.5 to 85 KDa) and isoelectric point (4.0 to 10.3 pI) (Chakdar et al. 2016). The optimal pH and temperature of the enzymes and their respective molecular sizes are presented in Table 7.2, for some microorganisms xylanase producers (Chakdar et al. 2016; Goswami and Pathak 2013; Walia et al. 2017).

Xylose is the most abundant pentose in nature, and it represents a suitable carbon source in microbial fermentation, is obtained by breaking the main xylan chain by the action of xylanases, as previously demonstrated. Moreover, xylose is an important source to obtain a great variety of high added products of importance to different industrial sectors (Table 7.3), such as the pharmaceutical industry.

## 7.6 Improvement of Xylanase Production and Purification

Xylanases can be produced by submerged fermentation (SmF) techniques or via solid-state fermentation (SSF). The fermentation process used will depend on the type of microorganism. Since fungi can grow at relatively low water activities, SSF conditions are more suitable for them than for bacteria Submerged fermentation is well-known for the production of xylanase and the control of the fermentation conditions is easier in this method. However, enzyme productivity is usually higher in SSF (Motta et al. 2013).

To obtain a satisfying xylanase production, the choice of substrate is of great importance. Depending on the substrate, the quantity and quality of the fermentation product can vary. Purified xylan (commercial product) is an excellent substrate because they increase xylanase yield by selective inducing xylanase without inducing cellulase production. The disadvantage is that this substrate has a very high cost, therefore, for the process to be economically viable, alternative substrates from agroindustrial waste such as sugarcane bagasse, wheat bran, corn cob, rice bran, etc., have been used (Chakdar et al. 2016; Bhardwaj et al. 2019b).

In filamentous fungi, substrates containing xylan induce the expression of the xylanolytic system. With xylanases production by the fungi, xylooligosaccharides are released, and the XOS induce the expression of other xylanolytic enzymes. The effect of oligosaccharide degree of polymerization on the induction of xylan-degrading enzymes by *Fusarium oxysporum* f. sp. *lycopersici* was evaluated. Results showed that compared to other xylanases production inducers such as sophorose, lactose, and cellooligosaccharides, the xylooligosaccharides are the best inducers of endoxylanase and β-xylosidases. A correlation was found between the degree of polymerization and enzyme induction efficiency since xylotetraose was the best substrate to induce endoxylanase production and xylobiose was the best inducer of cell-bound β-xylosidase (Najjarzadeh et al. 2020).

Different strategies can be employed to improve the yield production of the desired enzyme. The process can be optimized by the nutrient concentration in media, regulation of physical growth parameters (temperature, pH, agitation, incubation period), and use of biotechnology to improve producing-xylanase strains (Sharma 2017). A common approach for the selection of these important parameters is the one factor at a time (OFAT), in which just one parameter is variable and the others are kept constant (Bhardwaj et al. 2019b). Moreover, a response surface methodology (RSM) is used to optimize and understand parameter interaction.

The effect of substrate composition and temperature parameters was evaluated to improve xylanase production under solid-state fermentation by *Aspergillus fumigatus*. Using the OFAT approach, the highest xylanase activity was achieved using a combined substrate of sugarcane bagasse and wheat bran (1:1 w/w) at 45 °C (Gomes et al. 2016). An improvement of 3.2-fold was obtained after optimizing conditions for *Fusarium sp*. xylanase production. Different substrate and concentrations, the addition of carbon and nitrogen sources on the medium and physical parameters were evaluated by the OFAT approach and it was possible to reach a high xylanase yield of 4200 U/mL (Ramanjaneyulu et al. 2017).

Media optimization using OFAT enhanced xylanase from *Aspergillus oryzae* extracellular production by 5.7 times. Different media were tested by altering the concentration of the inorganic components. The non-optimized media presented xylanase production of 225 IU/mL, whereas after optimization xylanase production was up to 1290 IU/mL (Bhardwaj et al. 2018). Evaluation of several nutritional and physical parameters for xylanase by *Aspergillus fumigatus* strain was performed using the OFAT approach. The highest xylanase activity was obtained by sorghum hemicellulose as substrate at 2% (w/v), incubation temperature of 30 °C, agitation of 150 rpm, 1% (v/v) inoculum concentration, 50 mL volume of medium in 250 mL flask, and initial pH medium of 7 (Ravichandra et al. 2016).

Optimization using OFAT approach requires a large number of experiments and, consequently, more time to accomplish. Considering this fact, the statistical approach has been increasingly used. With a reduced number of design experiments taking into account different nutritional and physical parameters as variables and studying their interaction, this approach has presented satisfactory results for xylanase production optimization (Bhardwaj et al. 2019b).

After preliminary studies by OFAT, response surface methodology (RSM) was employed to optimize the production of xylanase, β-xylosidase, and β-glucosidase by *Colletotrichum graminicola*. Good levels of all enzymes were produced simultaneously using wheat bran as substrate at temperature and pH of 65 °C and 5.0, respectively (Zimbardi et al. 2013). The optimization of two nutritional and five physical parameters to improve xylanase from *Aspergillus niger* production was reported using the RSM approach. Only the parameters of substrate concentration and moisture content showed a statistically significant effect on xylanase production. Initially, xylanase activity was 2.93 U/g and after optimized conditions, it reached 5.23 U/g, which means that production increased 78.5% (Tai et al. 2019).

Optimization of some fermentation parameters such as media composition, pH, and temperature was performed by response surface methodology. Before optimization, *Aspergillus niger* ADH-11 produced at most 22.14 U/g of α-L-arabinofuranosidase. After performing the experiments, the results indicated that a temperature of 55 °C, pH 4, and wheat bran as substrate were the optimal conditions for maximum enzyme production. The yield of α-L-arabinofuranosidase was increased by 2.34-fold after optimization of fermentative parameters (Patel et al. 2015).

For industrial production and application of xylanases, a high yield of enzymes with specific properties such as stability over a wide range of pH and temperature, high substrate specificity, and resistance to chemicals and metal cations is necessary. However, most native xylanases reported are produced in low quantities and do not present these important characteristics required by industry. Therefore, a biotechnological approach can be applied to enhance xylanase production and add desirable characteristics to the enzyme. Technologies involving genetic manipulation such as mutations and recombinant DNA can be used for these purposes (Motta et al. 2013; Selvarajan and Veena 2017; Bhardwaj et al. 2019b).

Strains of *Aspergillus brasiliensis* and *Penicillium digitatum* were submitted to physical and chemical mutagenesis to enhance the fungus ability to produce xylanase. After physical mutagenesis with UV irradiation for 50 min and chemical mutagenesis with 150μg/mL of *N*-methyl-*N*′-nitro-*N*-nitrosoguanidine or ethyl methanesulfonate, xylanase activity of both fungal strains improved at least 30% (Popa et al. 2017). A protoplast fusion of two *Trichoderma* strains resulted in fusant presenting a 4.7-fold increase in xylanase activity compared to the parents. Results of a qPCR analysis showed that relative expression of the xylanase encoding gene increased by 4.9-fold (Zahra et al. 2018).

To improve xylanase activity from *Streptomyces* L10608, four amino acid residues were replaced by site-directed mutagenesis. Enzyme hydrolytic activity was improved 1.25-fold and presented a higher affinity for beechwood xylan as substrate (Xiong et al. 2018). After site-directed mutagenesis, the mutants of *E. coli* β-glucuronidase producer strain showed between three and fivefold increases in enzyme activity compared to wild type. Structural analysis showed that the mutation stabilized enzyme conformation, therefore facilitating effective binding on the substrate (Zhang et al. 2018).

Site-directed mutagenesis was performed to improve the activity of an alkaline stable and high-temperature tolerant xylanase from *Bacillus pumilus*. The mutant was expressed in *E. coli* and presented xylanase activity 1.5-fold higher at 60 °C. The mutant expressed in *Pichia pastoris*, which remained stable for 30 min at 60 °C, was optimized based on codon usage bias in order to further increase expression level. After codon optimization, strain Y16 showed an increase of 7.5-fold of enzyme activity. A qPCR analysis revealed that this strain presented 9 copies of the recombinant gene in the genome (Lu et al. 2016). By the same technique, endoxylanase gene from *Aspergillus usamii* was optimized and expressed in *P. pastoris*. Xylanase activity of the optimized gene was 59% higher than wild-type gene (Wang et al. 2016).

Catalytic performance and thermostability of a GH10 xylanase were enhanced by the fragment-replacement-based technique. Substitution of some fragments and their combinations improved catalytic efficiency up to fourfold and increased stability temperature up to 4.7 °C (You et al. 2019). Deletion of *Aspergillus nidulans* genes with predicted function enhanced homologous GH10 xylanase. The knockout of glycosyltransferase (pbnA), thioredoxin (trxA), cyclophilin (cypA), and hsp40co-chaperone (ydjA) genes improved homologous production of xylanase by 78, 105, 125, and 171%, respectively. Total protein secretion was affected by the gene deletions and decreased, indicating that it occurred a specific alteration for the production of homologous xylanase (Zubieta et al. 2020).

Two GH11 xylanase genes from thermophilic fungus *Myceliophthora thermophila* were cloned and expressed in *Pichia pastoris*. Both enzymes presented yield in 7.5 L fermentor, optimal activity at 60 °C with pH between 6.0 and 7.0, and their activities were not affected by EDTA and metal ions, meaning that they have important properties for use in industry (Basit et al. 2018). GH11 xylanase gene isolated from *Bacillus brevis* was expressed in *E. coli*. The recombinant enzyme was active under a wide range of temperature and pH, however, optimal activity at 55 °C and pH 7. In addition, the xylanase recovered 90% of activity when returned to 55 °C after boiling for 5 min, demonstrating thermostability (Goswami et al. 2014). A xylanase encoding gene was retrieved from a metagenomic library constructed from DNA extracted from compost-soil and expressed in *E. coli*. The recombinant xylanase presented activity over a wide range of temperature and pH and optimal conditions at 80 °C and pH 9.0 (Verma et al. 2013).

For their growth and development, microorganisms produce several enzymes and metabolites along with the enzyme of interest. Therefore, a purification process is necessary to remove impurities and obtain a pure enzyme. Different strategies can be applied for xylanase purification, such as ammonium sulfate precipitation followed by dialysis, ion-exchange chromatography, gel filtration chromatography, affinity chromatography, aqueous phase chromatography, and ultrafiltration. In order to obtain a good purification fold, these techniques are often combined (Bhardwaj et al. 2019b).

For enzyme precipitation, an adequate ammonium sulfate concentration (30–90%) needs to be selected. After precipitation, the enzyme is subjected to dialysis for salt removal. Xylanase produced by bacteria from sea sediment was partially purified by ammonium sulfate precipitation followed by dialysis. Precipitation of crude xylanase occurred with 40% ammonium sulfate saturation and dialysis was performed with sodium phosphate 0.05 mol/L pH 6 buffer. The specific xylanase activity improved after partial purification and the enzyme was characterized for optimum temperature and pH (Kumar et al. 2018).

A multi-step process where enzyme precipitation is followed by chromatography techniques is usually observed. Xylanase produced by *Bacillus licheniformis* was purified by a two-step process. Ammonium sulfate precipitation, the crude xylanase presented 72.53 IU/mg specific activity. After anion exchange chromatography using DEAE-cellulose, a yield of 15.97% and increased 5.86-fold specific activity was obtained (Kumar et al. 2017). Thermostable alkaline xylanase from *Anoxybacillus kamchatkensis* NASTPD13 was precipitated by 80% ammonium sulfate and after dialysis, the specific activity of 5.96 U/mg and twofold purification was obtained. The concentrated product from dialysis was submitted to gel filtration using a Sephadex G-100 column. After this process, specific activity and purification fold were 32.98 U/mg and 11, respectively (Yadav et al. 2018).

A three-step process was necessary to purify xylanase from *Bacillus amyloliquefaciens*. Ammonium sulfate precipitation, ultrafiltration, and ion-exchange chromatography were applied to obtain a specific activity of 217.39 U/mg and fivefold purification (Kumar et al. 2017). However, each step in a purification process reduces enzyme recovery. Besides, the downstream process for enzyme production is approximately 60–70% of the total processing cost. Therefore, a single-step purification is more advantageous for an industrial enzyme production process (Bhardwaj et al. 2019b).

Crude xylanase from *Aspergillus oryzae* LC1 was submitted to different purification methods separately, in order to evaluate the purification fold of a single-step purification for each technique. Purification after ammonium sulfate precipitation, anion exchange chromatography, and gel filtration chromatography resulted in purification fold of 4.1, 3, and 6.6, respectively. Moreover, the yield obtained was 21%, 31.9%, and 78.7% for each single-step purification technique, respectively. Single-step aqueous two-phase system (ATPS), a liquid–liquid fractionation technique, resulted in 13-fold purification and 86.8% yield, which was much higher than the other purifications techniques (Bhardwaj et al. 2019a). A GH11 xylanase from *Aspergillus tamarii* was submitted to a one-step chromatography using a CM-cellulose column. The specific activity of approximately 1.215 U/mg, 7.43-fold purification, and 36.72% was achieved (Heinen et al. 2018). Immobilized metal affinity chromatography (IMAC) has been also used as a single-step process for enzyme purification. The specific activity of *Bacillus* sp. from soil termite abdomen xylanase increased from 0.56 to 5.45 U/mg and purification using this single technique resulted in a tenfold purification (Taddia et al. 2021).

Biomass hydrolysis enzymes such as xylanase, cellulase, and pectinases, correspond to approximately 20% of total global enzyme production. A cost analysis of each step involved in xylanase industrial-scale production is not available in the public domain. However, a techno-economic analysis of a recombinant β-glucosidase industrial production revealed that major cost is facility dependent

(45%), which are included costs not directly associated with the process. Raw materials (25%) and consumables (23%) also represent a large cost. Glucose and IPTG (isopropyl-β-D-thiogalactoside) represent 47 and 41% of raw materials cost, respectively. In addition, the significant cost of consumables is due to the ultrafiltration membranes, which correspond to 80% of total consumables cost. Labor-dependent (4%), utilities (2%), and waste disposal (1%) generate little expense in β-glucosidase production (Ferreira et al. 2018; Bhardwaj et al. 2019b).

## 7.7 Biosynthesis of Xylan

Around 10 years ago, new investigations started being developed to produce engineer plants for biofuel production that has modified xylan improving its properties through the regulation of enzymes from Golgi apparatus (such as *glycosyltransferase* and *xylosyltransferase*), since xylan is synthesized in plants by the process that occurs in the Golgi apparatus (Rennie and Scheller 2014). Xylan is mainly produced in the secondary cell wall (SCW) during xylem development, which requires massive up-regulation of hemicellulose (e.g. glucuronoxylan) biosynthesis in the Golgi apparatus (Meents et al. 2019).

On the other hand, metabolic changes on xylan biosynthesis and modification are poorly understood (Wierzbicki et al. 2019). To date, there are several reports in the literature about the enzymes that are involved in the xylan biosynthesis and their respective functions, such as (1) *Xylan xylosyltransferases* (GT47), involved in the stretching of the xylan skeleton; (2) *Xylan glucuronyltransferases* (GT8), responsible for catalyzing the addition of GlcA in xylan, (3) *Xylan acetyltransferase*, catalyst in xylan monoacetylation, (4) *Glucuronoxylan methyltransferases* (DUF579), catalyst for GlcA methylation, among others (Zhong and Ye 2015). In any case, regulation of xylan biosynthesis has the potential to be a future alternative to obtaining products with high added value.

## 7.8 Concluding Remarks

In addition to being one of the most abundant raw materials in nature, hemicellulose can be obtained from agroindustrial waste. Therefore, hemicellulose is a renewable and sustainable source for converting into high value-added products, and biofuels. This bioconversion involves the action of enzymes that hydrolyze the main chain and the pendant groups of hemicelluloses from different biomass. Such enzymes are produced from bacteria and fungi, whether wild or via heterologous expression, and purified by different strategy of methodologies and techniques. These enzymes can be applied in the modification of the xylan chain, generating a polysaccharide with a specific pending group or degree of polymerization. The enzymatic modification can improve the xylan properties such as solubility or hydrophobicity. Xylan is raw material for different types of applications, and it can be converted into industrial products with high value-added (e.g. xylitol, lactic acid, levulinic acid, succinic acid, furfural, and bioactive compounds such as xylooligosaccharides) vida different routes. Therefore, knowing and producing both xylanases and accessory enzymes, acting separately or in enzymatic cocktail formulations, makes biorefinery and bioeconomics key processes to enrich technological and scientific advances for obtaining new products from hemicellulose.

**Acknowledgments** The authors thank the São Paulo Research Foundation (FAPESP grant number 2017/22401-8; 2019/12997-6; and 2018/07648-0) for financial support.

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# Hemicellulose Application for the Production of Bioplastics and Biomaterials

# 8

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## Abstract

Plastic has become a common material in society's daily life, since it meets industrial needs, due to its ability to be shaped in several ways, providing a relatively light, resistant, and inert product to be processed and manufactured on a large scale and at low costs. However, its environmental consequences over the years have caused several countries to deal with large amounts of residues, which accumulate for centuries without decomposing, thus affecting life in different biomes. An alternative towards the implementation of an efficient collection and recycling system would be its replacement (even if partially) with materials capable of degrading into small elements common to the environment. Hemicellulose, for example, is a polysaccharide highly available in the cell wall of plants, with potential application in the manufacture of biodegradable bioplastics that can replace conventional plastics; however, hemicellulose-based films are hydrophilic and have low mechanical resistance. There are challenges to improve the characteristics and fabrication processes of biodegradable films, which in addition to meeting market demands, must be viable. A great motivation is the strong market for functional materials such as packaging to promote better quality to the food. In addition, consumers are more demanding and concerned with the consumption of environmentally friendly products.

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M. Brienzo (ed.), *Hemicellulose Biorefinery: A Sustainable Solution for Value Addition to Bio-Based Products and Bioenergy*, Clean Energy Production Technologies, https://doi.org/10.1007/978-981-16-3682-0_8

**Keywords**

Biodegradable plastic · Biopackage · Xylan bio-composite · Mechanical property · Hydrophilicity · Compatibility

## 8.1 Introduction

Plastic has become one of today's biggest environmental problems, since it can remain undegraded for centuries and, associated with its large worldwide production, results in accumulations in landfills, dumps, and even in the environment. By the end of 2017, 9.2 billion tons of primary plastic was produced worldwide since 1950, and a large portion of this number is already waste (Geyer, 2020). An option for circumventing such an issue would be the use of the so-called bioplastics, which are alternative materials that meet the main industrial requirements and degrade in the environment.

The term "plastic," very widespread and used in our daily lives, does not refer to a single and particular material, just as "metal" does not refer only to iron or aluminum. It is employed for defining a range of materials of different structures, qualities, and compositions, whose common characteristic is their formation from the entanglement or chaining of long molecular chains of high molecular mass, known as macromolecules (Michaeli et al. 1992). Another important characteristic shared by plastics is their deformability, i.e., the possibility of being easily molded under certain conditions of heat and pressure, irreversibly acquiring a new form (Chanda and Roy 2008; Chanda 2017; Michaeli et al. 1992; Rodriguez et al. 2014).

Macromolecules are chemically complex; they are comprised of small molecules, called monomers, which can form sequences of more than 10,000 units. Macromolecular structures are connected and formed through chemical bonds of small units, thus enabling the production of different structures from different monomers and with different arrangements (Fig. 8.1) (Hiemenz and Lodge 2007; Mano and Mendes 1999; Michaeli et al. 1992; Rodriguez et al. 2014). Macromolecules are formed through chain reactions of those monomers, which start with an initiating agent that promotes the formation of an active center (it can be an ion or a free radical). From this active center, new monomer molecules are added in a fast and successive way, producing a larger chain in continuous growth, with an active center at one of the two ends. Such a process persists until it is suddenly interrupted by a terminating agent, generating a terminal group (Hiemenz and Lodge 2007; Mano and Mendes 1999).

Plastics are the main representatives of "polymers" (from Greek, many parts), which are macromolecules with chemical units repeated in a standardized way along the chain. Therefore, it can be understood that all polymers are macromolecules, but not all macromolecules are polymers (Chanda 2017; Hiemenz and Lodge 2007; Mano and Mendes 1999). Hemicellulose, a sugar highly available in several biomasses and relatively little used by the industry, is among the various natural raw materials studied in bioplastic compositions.

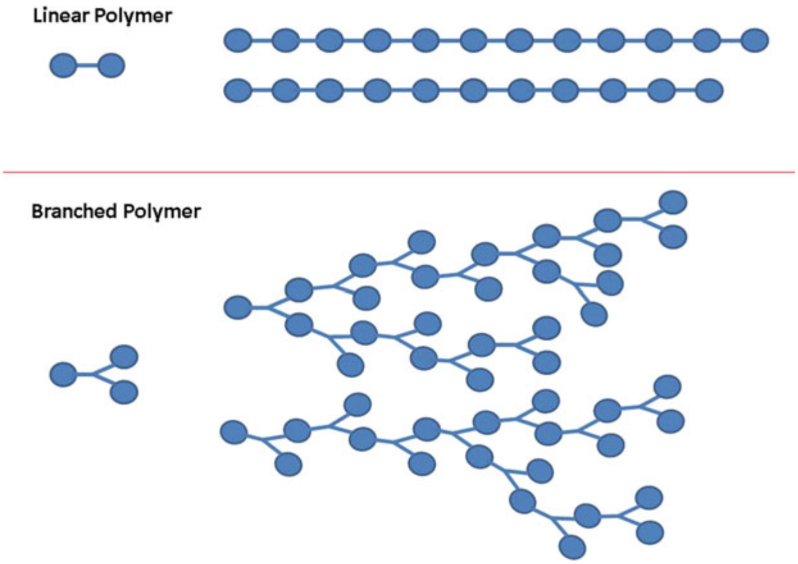

**Fig. 8.1** Polymeric chain models representing a linear polymer and a branched one

This chapter explores the reasons why plastics of petrochemical origin are so strongly present in society, and the environmental consequences of the dependence on this material. To then talk about bioplastics, defining what they are, their current market, and studies focused on bioplastics composed of hemicellulose. The main objective of this review is to indicate studies that suggest improvement of the hemicellulose properties for its application in the manufacture of bioplastics.

## 8.2 Plastic

### 8.2.1 Origin of Plastics and Their Importance for Society

Natural materials such as wood and several metals have been long used for the production of tools and objects for practical day-to-day tasks and protection, and as weapons. However, since society has evolved and its habits and needs have changed, such materials have become obsolete for certain applications, due to their lack of certain characteristics (e.g., lightness and easy processability).Therefore, new materials and processes of reduced costs have been required.

The progress of industrialization has demanded an increased use of electricity, hence, materials such as insulators for the production of electrical equipment and systems. Shellac, a resin secreted by an insect from Asia, has been widely used by industries as both an insulator and an ideal material for such applications. However, its availability is limited, due to its natural origin and production by insects at a rate lower than that required by the industry. In 1907, Belgian Leo Hendrik Baekeland developed the first synthetic plastic, called bakelite, from phenol and formaldehyde in his laboratory (Friedel 1984; Rodriguez et al. 2014).

The current idea of the polymer was drawn around 1920, when chemist Hermann Staudinger developed his structural model. Despite the lack of concrete evidence, Staudinger believed materials of chemical structure (unknown until then), such as natural rubber and some synthetic products, were made up of long molecular chains, differently from the idea they were colloidal aggregates of small molecules. Not only was Staudinger awarded the Nobel Prize in 1953, but also new materials started to be designed, thus contributing to the industrial development of the twentieth century (Mano and Mendes 1999; Michaeli et al. 1992).

Several properties (e.g., lightness) are responsible for the unrestrained use of plastics. Because they are lighter than other materials such as metals and ceramics, they are employed in the construction of airplanes and automobiles, and the production of sports equipment and packaging (Michaeli et al. 1992). Their processing requires lower energy expenditure and is easily conducted at a maximum temperature of 250 °C; in some cases, it can reach 400 °C, which is much lower than the 1400 °C required for steel, for example. This characteristic enables the integration of substances such as dyes, loads (wood and mineral powder), reinforcement loads (fiberglass or carbon), and foaming additives, responsible for improving the mechanical, thermal conductivity, optical, and insulating properties, as well as the material's density (Chanda and Roy 2008; Chanda 2017; Michaeli et al. 1992).

Although soluble in organic solvents such as gasoline and alcohol, plastics are good thermal and electrical insulators, since they resist certain chemicals and are less prone to corrosion than metals. They have variable permeability, and may or may not promote the diffusion of substances such as gases. Most of them are highly flexible when compared to natural materials (e.g., metals), and can replace glass, due to their higher resistance to impacts and similar optical properties (they can also be transparent materials) (Chanda and Roy 2008; Chanda 2017; Michaeli et al. 1992).

Coal had been the raw material for plastics until the mid-1950s, when it was replaced by naphtha, a portion of the oil refining, thus promoting industrial development, regardless of some falls over the years (e.g., the oil crisis, in 1973) (Nielsen et al. 2019; Michaeli et al. 1992). The success achieved by the alliance between plastics and petrochemical industries has resulted the fact that 99% of the raw material for the currently plastic production being based on fossil fuels. The plastic production is responsible for approximately 8 to 9% of global oil and gas consumption—specifically, 4 to 5% are used as raw materials and 3 to 4% are destined to power the production (Nielsen et al. 2019).

### 8.2.2 Negative Impacts Caused by an Irregular Plastics Disposal

Plastic has become an essential material in the infrastructure of modern societies, since it enables the production of several objects with different designs and applications, high resistance, lightness, and bioinertia at low costs (Nielsen et al.

2019). However, some of such good characteristics have led plastics to be one of the biggest current environmental problems.

Plastic pollution has reached different parts of the world, persisting on surfaces and in abyssal zones of oceans (Krause et al. 2020), soils, freshwater reservoirs, arctic ice (Bergmann et al. 2019), animal bodies, and the air (Windsor et al. 2019). The environmental spread of plastics is due to their persistence, since approximately 450 years are necessary for their disintegration—in some cases, they never reach complete degradation (Parker 2018). Another determining factor is their continuous and growing annual production. The worldwide plastic production has increased 200 times since 1950 and has continually grown at a 4% rate since the year 2000, with a production capacity estimated to grow 40% by 2030 (WWF 2019a). In 2018, 359 million tons of products were generated (Plastics Europe 2019). However, according to some reports, this number had already been exceeded in 2016, with 396 million tons (WWF 2019a).

The three most common worldwide destinations for plastic waste are recycling, incineration, and dumping, either in landfills and dumps or directly in the natural environment. From the development of plastic industry in 1950 to the year 2017, 7 billion tonnes of the 9.2 billion produced is waste, in which only 0.7 billion have been recycled while 5.3 billion was discarded in landfulls, dumps or natural environment (Geyer, 2020). Barriers have hampered the implementation of an efficient recycling system, hence, a significant share of recycles. One of such obstacles is the wide diversity of materials and formats, since functional innovations beneficial for their application tend to decrease the quality of the recycled material and increase both difficulty and value of the process. Other barriers include fragmentation and disorganization of the collection and classification system, which hamper a unified, articulated, and more efficient process with a consistent delivery flow of high-quality material to the recyclers (Ellen MacArthur Foundation 2016b).

In addition to difficulties in the waste management faced by most countries, recycled materials are devaluated on the market, because their quality is sometimes considered lower. Studies have suggested the contamination and mixing of different types of polymers can lead to secondary plastics of lower technical and economic values, thus limiting the reuse of some materials (Geyer et al. 2017). Although recycling is economical in some packaging applications, such as polyethylene terephthalate (PET) bottles, the cost of collection and sorting exceeds the revenue generated (Ellen MacArthur Foundation 2016b). In other words, the problem goes beyond the arduous exercise of population awareness. Such contexts hamper our devising a reality where the recycling of those wastes, considered the most appropriate way to treat them, can be compared to or even accompany the rate of plastics production. The rate tends to increase over the years towards meeting society's consumption demands, whereas the percentage of recycled waste will possibly remain unsatisfactory.

Optimistic data collected in the 28 countries of the European Union, Norway, and Switzerland, and presented by Plastics Europe (2019), a trade association representing the plastics industry in Europe, have highlighted a 92% increase in the recycling of plastic packaging between 2006 and 2018. However, still, only 42%

of the materials are recycled, while worrying 39.5% are represented as "energy recovery," a process characterized by the incineration of materials, which can cause other problems to both the environment and the incinerators health. Such an increase in the recycling rate is far from being a reality for the vast majority of countries.

In 2014, Europe and China showed high recycling rates of 30% and 25%, respectively, although incineration rates have also increased 40% and 30%. This recycling rate is better than those of countries like the USA, which from 2012 to 2014 have remained at the same 9% (Geyer et al. 2017). The difficulties in achieving an effective management faced by Europe countries and China are due to a complex task that involves waste reduction, adequate waste collection, classification of types of plastics, and improvement in recycling logistics (Nielsen et al. 2019).

Much of the waste for recycling in Europe is exported for processing (Nielsen et al. 2019). Although this practice is an environmental solution and offers economic advantages for underdeveloped and developing countries, it is not effective, since such importing countries have been overburdened. Consequently, China, which had an important function in recycling waste from other countries, restricted the import of waste in 2018 (Brooks et al. 2018), leaving its role vacant for Southeastern Asian countries that already import waste from some countries of the Organization for Economic Cooperation and Development (OECD). However, many of those Asian countries do not have a proper infrastructure for managing their own wastes (Brooks et al. 2018).

Some applications for plastics generate more waste and are more alarming. Approximately 42% of non-fiber plastics, comprised predominantly of polypropylene (PP), polyethylene (PE), and polyethylene terephthalate (PET), have been used for the production of packaging, while 19% have been employed in construction materials. However, such applications generate 54% and 5% of wastes, respectively. Certain products (e.g., disposable objects) are manufactured on a large scale and discarded in the same year of production. On the other hand, plastics used in construction have relatively low production and are generally discarded after decades (Geyer et al. 2017). Therefore, depending on the application and type of plastic, efforts are devoted to solving urgencies considered imminent threats to the environment.

Disposable materials such as packaging, supermarket bags, bottles, straws, containers, cups, and cutlery are the most problematic among plastic wastes (UNEP 2018), not only because they become waste quickly, but also because they are the most produced plastic materials. Among them, packaging currently represents 26% of the total volume of plastics used by the industry (Ellen MacArthur Foundation 2016a). The ubiquity of those materials in the environment is related to a relatively cheap production and the recent demand of society for individual and practical food products. The Brazilian Association of the Industry of Food for Special Purposes and Similars pointed out a 4.9% increase in sales of ready and semi-ready dishes and frozen and dehydrated foods in 2019 (ABIAD 2020). The Brazilian Association of the Industry of Food for Special Purposes and Similars pointed out a 4.9% increase in sales of ready and semi-ready dishes and frozen and dehydrated foods in 2019 (ABIAD 2020). The effect of the pandemic originated in

2019 due to the SARSCoV-2 virus, responsible for developing a respiratory crisis in humans that can lead to death, must also be considered. Because the use of personal protective equipment (PPE), such as masks and gloves, has become an important public health tool to prevent the spread of the virus in the population. As a result, there was a significant increase in the use and consequent disposal of these equipment that are made of plastic, for example, at King Abdullah University Hospital in Jordan, where it is estimated that ten times more medical waste is produced (approximately 650 kg/day) than in any period prior to the pandemic. The same is reported in other countries, such as Spain and China, which had an increase of 350% and 370% in the production of hospital waste, respectively. This leads to a particular problem regarding the handling of this potentially infectious plastic waste, because the sorting and recycling of these materials is avoided to ensure the health of employees at recycling facilities. There are only two options for the disposal of this waste, incineration, which ends up being the most practiced by many countries, especially the more developed ones, and disposal in landfills or even dumps (Patrício Silva et al. 2021). Due to the pandemic, the demand for plastic is still expected to grow by 17% in applications like medical uses and 40% in packaging due to consumer demand for more packaged fresh food, because they believe that are better protected from SARS-CoV-2 contamination. Thus, the development of PPE from bioplastics, in addition to be an environmentally more suitable alternative, would also prevent the spread of the virus through waste, because viable SARS-CoV-2 persists longer on plastic surfaces than on other materials (Patrício Silva et al. 2021).

Environmental problems arise when plastic products are incorrectly disposed of. Although the flow of plastic waste among different systems (atmospheric, terrestrial, and freshwater) is multidirectional, marine systems are generally the final destination (Windsor et al. 2019). More than 5 trillion plastic particles, i.e., over 250 thousand tons are estimated only on the surface of oceans (Eriksen et al. 2014).

Much of the plastic pollution is correlated to human activity in terrestrial environments. Plastic particles can be easily transported by the action of the wind, since they are light materials. Running water also contributes to the distribution of plastic waste; it acts as a conduit that connects terrestrial, freshwater, transition, and marine systems, providing an important long-distance transport route, and can also direct and store waste in benthic, floodplain or riverside habitats. When improperly deposited in the environment, plastics can be carried to river systems by the action of rainfall and through the leaching of the soil, thus representing a risk of contamination in freshwater environments (Windsor et al. 2019). Among the main sources of plastic waste in the soil are intensive agricultural practices, which distribute plastics in rural regions through the degradation of machinery, dissemination of garbage, application of sewage sludge in soil conditioning, and plastic coverings. Urban activities also act as a source of plastic in the environment, such as the waste disposal in landfills and dumps and industrial spillage (Windsor et al. 2019).

As addressed elsewhere, oceans are considered the endpoint of the plastic flow of hydrographic basins, responsible for a large amount of plastic wastes disposed of in the marine environment. However, a significant quantity is likely to be sent directly into the oceans, since 50% of the global population reside 31 km from the coast. Industrial activity and commercial fishing also contribute to the accumulation of plastics in marine ecosystems (Windsor et al. 2019). According to an analysis conducted by the Ellen MacArthur Foundation (2016a), if the current ratio of plastic disposal that reaches the oceans remains, more plastics (850–950 million tons) than fish (812–899 million tons) will be found in the ocean (in relation to the mass) by 2050.

Plastics are encountered even in the air due to their lightness, which enables them to be suspended and transported to the atmosphere. They can come from hydrographic basins, combustion of plastic waste, wind erosion from different media, urban dust (tire wear particles, paint, and synthetic fibers), and waste dispersion (Windsor et al. 2019). In the environment, the most obvious impact of plastic pollution on an ecosystem is asphyxiation in large and small animals (Windsor et al. 2019). Images of animals trapped in plastic discards are commonly found; such a fact is not exclusive to marine environments, since American crows have shown evidence of strangulation (Windsor et al. 2019). More than 690 marine species have ingested some plastic material (Provencher et al. 2017) that can harm them in many ways. For example, the ingestion of some plastic waste can either lead to death by choking or give a false sense of satiety, reducing the absorption of nutrients, causing changes in the intestinal microbiota, and consequent reduction of energy provisions. All such outcomes lead the animal to exhaustion, reducing important activities for it to stay alive and reproduce (Windsor et al. 2019).

Apart from physical impacts, which are more easily observed, indications of chemical impacts from exposure to plastics have also been reported. Because plastics are complex products, they can adsorb contaminants from the environment, or leach their various additives, which act as flame retardants, plasticizers, hardeners, surfactants, and synthetic dyes. These chemical components are released over time and can be potentially toxic to the environment (Windsor et al. 2019).

Sea turtles are some of the most affected animals by the impact of plastic waste. Ingestion occurs mainly because they confuse waste with possible food (e.g., plastic bags with jellyfish (Carr 1987) or seagrass (Duncan et al. 2019b), and are attracted by the smell of organic matter from microorganisms that develop and die on the surface of the plastic (Pfaller et al. 2020)). In a study with individuals from seven species of sea turtles sampled from three ocean basins (Atlantic, Mediterranean, and Pacific), Duncan et al. (2019a) observed all organisms analyzed had synthetic particles, of which most were fibers, followed by fragments and microspheres. Such particles were found in species that occupy different trophic levels, indicating those materials can be ingested through multiple routes, including exposure to plastic pollution in the marine ecosystem and trophic transfer.

Plastics of 1 μm to 5 mm are called microplastics (they can be even smaller, and, therefore, called nanoplastics) and are found in different places (e.g., depths of the Mariana trench and the Arctic ice). Most of them result from the degradation of larger plastics, although, in some cases, they are intentionally produced by industries, such as cosmetic ones (Nielsen et al. 2019). Their presence in the marine ecosystem impairs its oxygen production, interfering with the growth of *Prochlorococcus,* the most abundant photosynthetic bacteria in the oceans.

Therefore, their deposit in the oceans can lead to both deficiencies in oxygen production and absorption of carbon from the environment (Tetu et al. 2019).

Humans are not exempt from possible damage to health caused by plastic waste, due to evidence of transfer of microplastics through the aquatic food chain. Such a bioaccumulation is a major threat to predators at the top of the food chain, like humans (Wang et al. 2019). The bioaccumulation of plastics was evaluated by Cheikh et al. (2018) in scallop (*Pecten maximus*), a mollusk commonly appreciated as a refined food. The animal showed rapid uptake of nanoparticles, which accumulated in the intestine and throughout the body after 6 h of exposure, remaining in the mollusk after 48 days.

A study from the University of New Castle, in Australia, revealed an ordinary person can ingest 5 g of microplastics weekly, which is equivalent to the mass of a credit card. According to the study, such materials are ingested through the consumption of drinking water, beer, seafood, and salt (WWF 2019b). This finding was corroborated by results achieved by researchers in the Czech Republic, who analyzed water samples and found microplastics at 1473 to 3605 particles/L of raw water and 338 to 628 particles/L of treated water. In general, the particles were smaller than 10μm, with a predominance of fragments and fibers mostly composed of PET (polyethylene terephthalate), PP (polypropylene), and PE (polyethylene) (Pivokonsky et al. 2018). Likewise, a Chinese study found 550 to 681 particles/kg in sea salts, 43 to 364 particles/kg in lake salts, and 7 to 204 particles/kg in rock or well salts, mostly characterized by fragments and fibers measuring less than 200μm. The most common microplastic was PET, followed by PE and cellophane (Yang et al. 2015).

Small particles negatively affect fish's reproductive system (Nielsen et al. 2019), as well as humans exposed to components used in plastics, such as phthalates, bisphenol A (BPA), polybrominated diphenyl ethers (PBDE), and tetrabromobisphenol A (TBBPA). Phthalates and PBDE act as anti-androgens, BPA has estrogen-like activity, and PBDE and TBBPA can disrupt thyroid hormone homeostasis (essential for normal neurological development and reproductive function). Such compounds can act on hormonal disorder mainly in childhood; since the child's organism is still under development, it is more sensitive to external interferences. Kovanecz et al. (2014) and Talsness et al. (2009) reported testicular dysgenesis syndrome in male rats after perinatal exposure to phthalates caused by prolonged exposure and accumulation of those compounds in the body, similarly to what is observed in humans.

Evidence has pointed to possible cytotoxic effects of nanoplastics on human blood cells, due to the affinity between plasma proteins and the nanoplastic, leading to conformational changes in the protein, hence, its denaturation and bio-incompatibility. Gopinath et al. (2019) reported indications of genotoxic effects while studying onions (*Allium cepa*), whose root growth was hampered by the exposition to nanoplastics, leading to chromosomal aberrations.

The potential cytotoxicity of micro and nanoplastics can be combined with other compounds, forming reactive oxygen species (Schirinzi et al. 2017) that transport metals in the marine environment. In some cases, plastic pellets whose concentrations of remaining metals (Cr, Co, Ni, Cu, Zn, Cd, and Pb) exceeded those normally reported for local estuarine sediments (Holmes et al. 2012) were detected. Another risk is microplastics acting as vectors for the dispersion of pathogenic microorganisms such as *Vibrio* spp adhered to the plastic surface through a biofilm (Kirstein et al. 2016).

Plastic production is potentially polluting. In 2016, it generated approximately two billion metric tons of $CO_2$ emissions, corresponding to 6% of the emissions of this gas per year, thus intensifying the greenhouse effect (WWF 2019a). A significant amount of greenhouse gases will still be emitted, since large volumes of plastics are broken down into smaller pieces, also leading to acidification of the oceans, loss of biodiversity, and the ability of this ecosystem to absorb carbon (Nielsen et al. 2019).

Socio-economic problems could be more effective to alarm society about the problem of waste accumulation on the planet than threats to the environment, to the health of fauna of humans. The fishing activity for both commercial and recreational purposes shows the negative impacts generated by plastic wastes through the reduction of its productivity and damage caused to fish (Windsor et al. 2019). According to Mouat et al. (2010), the activity of 86% of Scottish fishing vessels had been harmed by marine litter. Despite the relatively low concentration of contamination, the ingestion of microplastics by fish and seafood can also exert a negative economic impact through the bad impression conveyed by the products to consumers (Windsor et al. 2019).

Plastic waste also affects tourism in natural environments, since pollution impairs the visual appeal of the place and represents a risk to the well-being of tourists. Approximately 70% of marinas and ports for leisure reported their users had already suffered an incident with solid waste (Mouat et al. 2010). Water treatment systems also suffer financial losses due to plastics improperly discarded, which end up in the pipes and equipment, damaging them and causing obstructions. Treated water suppliers are forced to invest and look for solutions that adapt their infrastructure to this current problem (Windsor et al. 2019).

Modern society has assumed a certain dependence on plastics, as in the case of food packaging, which protects and maintains the desirable qualities of a product for the consumer and increases its both longevity and hygiene (Nielsen et al. 2019). However, the problem caused by the unrestrained use and irresponsible disposal of that material is evident. Environmental awareness and the adequate handling of plastics through an efficient recycling system have proven the most prudent and thoughtful solution, although it is still a difficult reality and very far from being reached. Consequently, the replacement of part of plastics with biodegradable materials has motivated studies on the use of biomaterials instead of conventional plastics.

## 8.3 Bioplastics

### 8.3.1 Origin of Bioplastics

Evidence has shown man has used natural materials obtained from plants from the very beginning. Gums, for example, are substances formed by polysaccharides and their derivatives, characterized by colorless, odorless, tasteless, non-toxic, and capable of forming viscous solutions or even gels (Mano and Mendes 1999; Pereira et al. 2012). They were used for years to join pieces of wood in buildings or to waterproof boat surfaces (Lackner 2015). Gum Arabic, a secreted resin from Acacia trees used by the Egyptians in 2000 B.C. as an adhesive in the mummification process and mineral paints is still used mainly by the food and pharmaceutical industry (Musa et al. 2018).

There is no doubt about the importance of the industrialization process for the development of new materials. In the beginning, once the understanding of chemistry was still relatively limited, the industry took its first steps using and studying completely natural materials. The progress of chemistry, combined with the application of those organic materials, has promoted the development of new bio-based products with increasingly interesting properties. One of the major findings is attributed to Charles Goodyear, who, in 1839, discovered the process of vulcanization of natural rubber, a polymer derived from a milky colloidal suspension called latex and found in certain tree species. The process enables the addition of sulfur to the polymeric rubber chain at high temperatures, making it more resistant and elastic (Costa et al. 2003; Lackner 2015). The discovery of this thermoset material, which can be molded only once after being heated and cooled, encouraged the search for new polymers, resulting in the creation of thermoplastic materials that can be remodeled several times.

The 1862 London International Exhibition presented Parkesine, the first plastic material, produced by English Alexander Parkes. It was biobased, due to its formation from cellulose nitrate derived from cotton, in which the cotton cellulose was treated with nitric and sulfuric acid and then mixed with vegetable oil and organic solvents (Lackner 2015; Lintsen et al. 2017; Quye 2017; Vincent 2006). In summary, the polymer is formed because the cellulose has hydroxyl side groups (–OH) that are replaced by nitrate groups ($NO_3$–) through an esterification reaction with an aqueous acid mixture. Consequently, the acid concentration of the mixture determines the degree of substitution of the groups, and plastics with different properties are produced. For example, moldable plastics were obtained with 10.5% nitrogen content of the final product, and films were made with 11.5%. However, a material with explosive characteristics could be obtained (Quye 2017) with a slightly higher content, i.e., approximately 13.5%.

Thermoplastics were a great novelty for that time, and their consistency was similar to that of dough, which could be shaped in different ways when subjected to heat and pressure. Parkesine was described as “hard as a horn, flexible as leather, capable of being cast or printed, painted, dyed or sculpted” (Vincent 2006), thus showing the dependence on the referenced materials (e.g., horn, leather, ivory), currently considered more rustic, and the novelty thermoplastics represented, as well as the greater possibility of producing materials of different shapes and colors, important for the industry. However, Parkesine was still relatively fragile and brittle; its production was impaired and interrupted after 2 years due to its high costs, forcing manufacturers to produce a lower quality material (Lintsen et al. 2017; Quye 2017). Despite the failure of Parkesine, researchers continued to look for new materials, and some of them, such as celluloid, caught the attention of the industry (Lintsen et al. 2017; Quye 2017; Vincent 2006).

The origin of celluloid is related to a contest held by American company Phelan and Collander in the middle of 1870, towards finding a cheaper substitute for ivory, extracted from elephants, for the production of its billiard balls. American researcher John Wesley Hyatt applied the same cellulose nitrate technique used by Parkes, but adding camphor as a plasticizer and ethyl alcohol as a solvent. Although the use of flammable reactants, a more stable than Parkesine and ideal material for the industry was created (Canto 2004; Lintsen et al. 2017; Quye 2017; Vincent 2006; Rodriguez et al. 2014).

Industries have always aimed at larger, cheaper, and higher-quality productions, and, because of the discoveries related to cellulose nitrate plastic, have developed more and more materials synthetically and based on fossil fuels. Like naphtha, a cheap raw material, that enabled a massive production of petrochemical polymers in the 1940s and 1950s. Due to these circumstances, the industry was moving towards a more synthetic route similar to what occurred with bio-based fuels, which were replaced by fossils such as gasoline and diesel (Lackner 2015).

### 8.3.2 Bioplastic Composition and Structure

Similarly to plastics of fossil origin, the structure of bioplastics is comprised of chains of macromolecules formed by monomers. Such chains are connected to each other resulting in a semi-rigid three-dimensional network structure, with the solvent trapped and immobilized between the bonds, as illustrated in Fig. 8.2. The degree of cohesion of the structure depends directly on the structure of the polymer (the polymeric chains that make up the network), the solvent used, the drying temperature, and the presence of other molecules, such as plasticizers. Polysaccharides of linear structure (e.g., cellulose, amylose, or chitosan) generate more resistant, flexible, and transparent polymers, and are an efficient barrier to fat and oils (Tharanathan 2003).

This network of biomolecules, in many cases called a polymer, can be classified according to the "meros" (from the Greek, meaning "parts") that form it. If made from a single type of unit, they are homopolymers; however, the concept here of pure polymers is different from that applied to chemistry in general, due to the difficulty in obtaining fractions of absolute molecular uniformity with biomolecules. On the other hand, polymers formed from more than one type of units are called copolymers. Copolymers are characterized as alternate, in case of perfect sequencing regularity, block, if, instead of a single chemical unit, there are sequences of equal

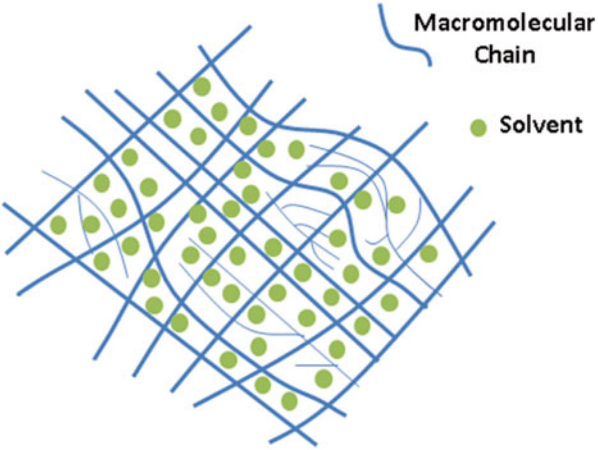

**Fig. 8.2** Illustration of a semi-rigid three-dimensional network structure

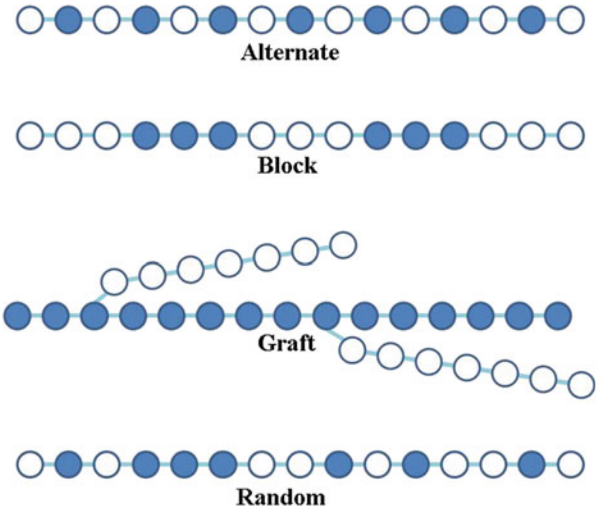

**Fig. 8.3** Types of copolymers

chemical units alternating (such specific blocks as polymeric branches are known as graft or grafted copolymers), and random copolymers, which, as the name implies, are formed by units with randomly arranged sequencing (Mano and Mendes 1999), as illustrated in Fig. 8.3. Hemicellulose, which will be further addressed, is an example of random copolymer, due to its both complex and random composition and sequence (Imre et al. 2019).

Bioplastics are characterized by the European Bioplastics Industry Association as being biobased or biodegradable or both. The European Committee for Standardization also brings as a criterion to bioplastics the biocompatibility of these materials, which allows them to be applied in medical therapy (Imre et al. 2019). They are bio-based materials if their constitutional units are totally or partially originated from biomass. They can be natural, synthesized by living organisms, or even bio-based synthetics, whose monomers are derived from biological sources. Another characteristic of bioplastics is their ability to be biodegraded in the environment. The biodegradation process transforms organic matter into final smaller inorganic molecules such as $CO_2$ and $H_2O$, a process known as mineralization. The process takes place from the action of enzymes released by living cells (usual microorganisms), and is often accompanied and promoted by physical-chemical phenomena (Imre and Pukanszky 2013; Imre et al. 2019; Lackner 2015).

The bioplastic decompositions by microorganism action occur with a pool of enzymes that act on different types of hemicellulose (and its substituents) with different chain sizes, producing monomeric sugars, uronic and acetic acids. Such enzymes with different functions act synergistically in specific regions of the polysaccharide, such as endo-1,4-β-xylanase, which is used hydrolyzes xylan into oligosaccharides, and 1,4-β-xylosidase, which releases xylose monomers from oligosaccharides. Accessory enzymes (e.g., xylan-esterases, ferulic acid esterases, p-coumaric-esterases, α-1-arabinofuranosidases, and α-4-O-methyl glucuronosidases) generally act breaking the binds between the side groups and the main chain composed of xylan (Abe et al. 2021).

Bioplastics behavior towards the action of the enzymes must be considered, because it is important to estimate the time and conditions required for the material to be fully mineralized, proving its biodegradability. Although few studies have addressed the biodegradation of hemicellulose bioplastics, Lucena et al. (2017) proved bioplastics based on xylan blended with gelatin are fully biodegradable after 15-day conditioning in a mixture of soil and manure. However, the rate of biodegradation depends on the proportion of hemicellulose and the component it is mixed with. After buried for 30 days, films produced with beechwood xylan and polyvinyl-alcohol showed 42.2% and 56% biodegradation degrees, and 25 and 50% xylan concentrations, respectively, indicating xylan is more prone to enzymatic attack (Wang et al. 2014). In the same study, the authors observed the presence of citric acid in the bioplastics interfered with the degree of biodegradation, which decreased from 42.2% to 33.5%, due to the ester bonds formed when the cross-linker was present, hampering the attack of microorganisms, in comparison to hydrogen bonds (Wang et al. 2014).

Xylan bio-composites were produced with poly-(ε-caprolactone) (PCL), and a high biodegradation degree between 95.3% and 99.7% after 28 days of analysis was identified (Farhat et al. 2018). However, the biodegradation kinetics was different between films composed only of hemicellulose and those with PCL. The materials showed slower biodegradability kinetics when the PCL content was increased, probably due to the fact that this component has a higher degree of polymerization and substitution rate compared to hemicellulose.

Some types of raw material processing, such as chemical modification through acetylation, can also change the biodegradability degree of bioplastics. Fitch-Vargas et al. (2019) produced films based on acetylated starch and lignocellulosic fibers that showed an approximately 30% level of biodegradability in 5 weeks, suggesting, according to the authors, the bioplastic maintained reasonable stability. They also observed an increase in the fiber increased both crystallinity and recalcitrance of the bioplastic, hindering the access and action of degrading enzymes. However, all such results provide an estimate of the time required for bioplastics comprised of hemicellulose to degrade, since the diversity of microorganisms responsible for degradation and the conditions to which bioplastics are subjected can change the degradation rate. In all cases, hemicellulose proved capable of being biodegraded, and, depending on the desired application of the bioplastic, the addition of some polymers or chemical modifications can extend the time for the material to be converted into simpler compounds in nature (Gu 2003).

The characteristics that define bioplastics do not necessarily present themselves as adjuncts. In some cases, the material may be of biological origin, but not biodegradable, as is the case of bio-based polyethylene terephthalate (PET), polyamides, polyurethanes, natural rubber, and highly substituted cellulose acetate. On the other hand, bioplastics of fossil origin, such as polybutylene succinate, poly-ε-caprolactone, and polyvinyl-alcohol can be biodegradable (Imre and Pukanszky 2013; Imre et al. 2019; Lackner 2015).

Bio-based plastics are comprised of renewable materials, and can be produced from derivatives of organic molecules (e.g., biomass-based PET, formed through the polycondensation of ethylene terephthalate monomers, which are products of reactions between terephthalic acid (esterification reaction) or dimethyl terephthalate (transesterification reaction) with ethylene glycol). Based on this principle, Lackner (2015) and Mohsenzadeh et al. (2017) developed a PET using monoethylene glycol (MEG) derived from sugarcane ethanol. However, bio-based products can also be natural (e.g., polylactic acid (PLA) and polyhydroxybutyrate (PHB)). They are thermoplastic polyesters secreted by microorganisms, and enable large-scale production through fermentation in bioreactors (Imre et al. 2019; Pachekoski et al. 2014). Chitosan is also a macromolecule of biological origin widely used in the production of biodegradable films. Its excellent film-forming property, due to its numerous hydroxyl and amine groups, enables the formation of several hydrogen bonds. Obtained by the deacetylation of chitin present mainly in the cell wall of fungi and the exoskeleton of arthropods, it is biodegradable and non-toxic, with antioxidant and antimicrobial activity (Costa et al. 2015; Xu et al. 2019). Among natural materials are the macromolecules produced by plants, which have the advantage of being raw material obtained by an inexpensive way, since it requires only the ideal conditions for the development of plants. A wide diversity of plants rich in starch, lignocellulose, and pectin can also be applied in bioplastics production (Imre et al. 2019).

Most of the studies on biodegradable films are focused on the use of cellulose and starch in the composition of such films (Imre et al. 2019). Cellulose is the most abundant biopolymer on Earth, present in the cell wall of plants, along with two other main components, namely hemicellulose and lignin. Its structure is built from β (1–4) glycosidic bonds between ᴅ-glucopyranosyl units, forming long, linear polymer chains that, due to the hydroxyl groups in their structure, are grouped into microfibrils through intramolecular and intermolecular hydrogen bonds. Despite the partial presence of amorphous regions, the chain arrangement results in a material of high crystallinity degree (Mano and Mendes 2013; Shackelford 2004) that guarantees the characteristic resistance of cellulose (Coma 2013; Imre et al. 2019; Mano and Mendes 2013; Melati et al. 2019).

Starch is a vegetable storage polysaccharide, widely available in nature, found in cereals, tubers, pods, and roots (Botham 1995; Denardin and da Silva 2009; Keetels et al. 1996; Mano and Mendes 2013; Souza and Andrade 2000), and which displays two types of α-D-glucopyranose polysaccharides structures. One is amylose, a linear macromolecule joined by α(1–4) glycosidic bond, and generally found in lower quantity and mass than the second type, i.e., branched amylopectin, also characterized by α-type bonds (1–6) at branch points and α (1–4) (Denardin and da Silva 2009; Imre et al. 2019; Keetels et al. 1996; Souza and Andrade 2000).

Hemicellulose has been gaining attention of researchers in recent decades for composing between 15 and 35% of plant biomass (Naidu et al. 2018). It is a polysaccharide of partial solubility in water, but quite soluble in diluted alkaline medium (Alves et al. 2020; Freitas et al. 2019; Brienzo et al. 2016). It is associated with cellulose in the plant cell wall and can vary according to its composition and primary molecular structure, showing 80 to 200 sugar units polymerization degree. Its high complexity causes its composition to vary not only between plant species, but also between tissues and developmental stages in a same species (Ferreira et al. 2009; Freitas et al. 2019; Melati et al. 2019).

The structure of hemicellulose is comprised of different types of monosaccharides/compounds, including pentoses (D-xylose and α-L-arabinose), hexoses (D-galactose, D-glucose, and D-mannose), and uronic acids such as α-D-glucuronic, α-D-4-O-methylgalacturonic, and α-D-galacturonic. Like cellulose, its main chain is composed of monosaccharides (mainly glucose, mannose, and xylose) with β (1–4) bonds and branches of neutral sugars and uronic acids (Ferreira et al. 2009; Freitas et al. 2019; Imre et al. 2019; Melati et al. 2019). Due to its diversified composition and structure, hemicellulose has low crystallinity, characterized by its amorphous state and lower polymerization degree. Thus, showing less chemical and thermal stability compared to cellulose (Stepan et al. 2012). Hemicellulose whose main chain is formed by β (1–4) bonds of D-pyranose residues (hemiacetal sugars) is classified into three main groups, namely mannans, xylans, and xyloglucans (Fig. 8.4) (Naidu et al. 2018).

The main chain of mannans is formed by mannose units. Mannans are divided into four subgroups, namely linear mannans, galactomannans, glucomannans, and galactoglucomannans. The first subgroup is comprised solely of mannose residues and can be found in the endosperm of some plants, such as ivory nut and species of the Leguminosae family. Galactomannans are found in legume seeds, and their main chain consists of mannose units with lateral groups of galactose making α-1,6 bond at an above 5% rate—the higher the rate, the higher the hydrophilicity of the polysaccharide. Glucomannans are abundant in the secondary cell wall of woody species (mainly softwood), and their main chain is formed by β (1–4) bonds of mannose and glucose, whose rate substantially varies according to the source. They usually form chains with few branches, starting from the mannose units. Finally, Galactoglucomannans are also found in softwood, and their main chain is formed by

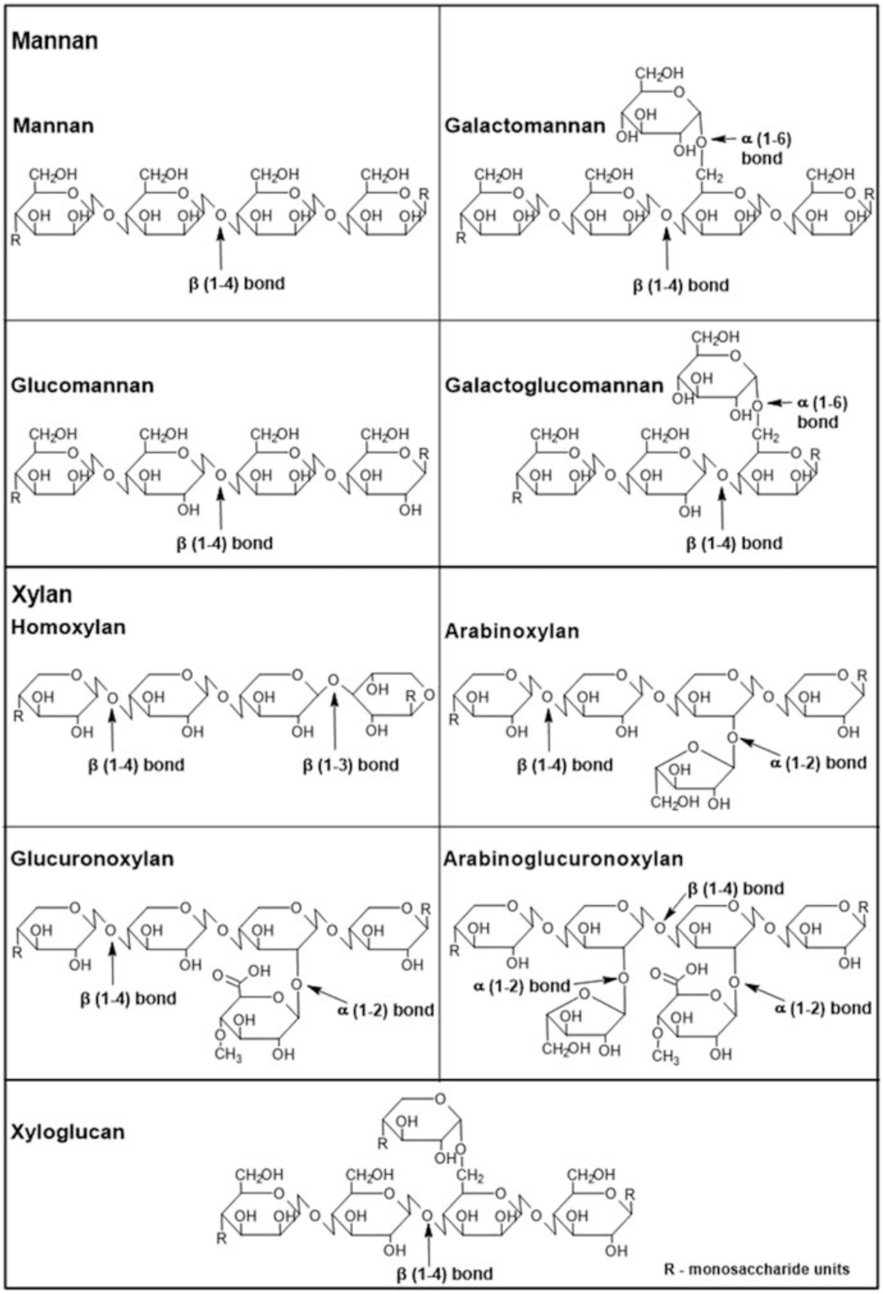

**Fig. 8.4** Groups of hemicellulose

mannose and glucose, with branches of galactose units. Similarly to galactomannans, galactose content and its degree of branching increase its solubility in water (Naidu et al. 2018; Stepan et al. 2012).

Xylan is the most common type of hemicelluloses (Freitas et al. 2019), present in hardwoods, grasses, cereals, and herbs (Ebringerová and Heinze 2000; Stepan et al. 2012). Its main chain is formed by D-xylose units through β (1–4) glycosidic bonds to which branch groups of L-arabinose, acetic acid, and uronic acids are attached (Deutschmann and Dekker 2012; Naidu et al. 2018). It also has subgroups determined by the source. The first is comprised of homoxylans, found in seaweed, and formed only by xylose residues, which may be linear or branched; therefore, they may have both β-1-4 and 1–3 bonds, as well as a mixture of them. The second group is composed of arabinoxylans, found in cereals. Their backbone is formed by xylose, with arabinose units being the main side group, attached to the carbon 2 or 3 positions of xylose units. However, carbon atoms in the same positions can be linked to acetyl groups. The rate of arabinose in relation to xylose is an important factor; since it influences the degree of sugar branching that will influence the polymerization degree.

The third subgroup is formed by glucuronoxylans, present in hardwood trees and whose main chain is composed of xylose residues, replaced every 10 units by 4-O-methyl-D-glucuronic acid. The chain also has partial acetylation on carbons 2 and 3, and these acetyl groups collaborate for the solubility of xylan. The next subgroup of xylans is called arabinoglucuronoxylan, found in non-woody plants, such as grasses and softwood. Its structure is characterized by the binding of arabinofuranose and glucuronic acid in the carbon of positions 2 or 3 of xylose that makes up the main chain. Approximately, substitutions with glucuronic acid and arabinofuranose occur every 5–6 and 5–12 xylose units, respectively, and the presence of ferulic and coumaric acids is associated with arabinose residues through esterifications (Naidu et al. 2018; Stepan et al. 2012).

The last subgroup is comprised of xyloglucans which, except grasses, are the most abundant hemicellulose in many plants. Their structure is similar to that of cellulose, i.e., formed by glycosidic bonds β-1-4 with xylose residues linked in position 6 of some glucose residues. They are highly branched, and arabinose and galactose units can be linked to xylose residues, forming di or triglycosyl side chains. This group substantially contributes to the structural integrity of the cell wall by making hydrogen bonds with cellulose (Naidu et al. 2018).

The presence of several side groups in the main chain of hemicellulose prevents molecules from forming a tight packaging, as it occurs with cellulose, influencing its amorphous characteristics, solubility in water, and interactions with other components in a film. In a hypothetical composition formed by hemicellulose and cellulose, the region of hemicellulose with least degree of substitution will closely interact with cellulose and form a less soluble region, also influencing other properties such as mechanical performance (Stepan et al. 2012). The side groups play an important role in the solubilization of hemicellulose. A high substitution degree chemically induced with acetyl groups also results in the removal of hydrophilic substituents, enabling polysaccharides to become more hydrophobic (Stepan et al. 2012).

### 8.3.3 The Bioplastics Market

The origin of plastics is related to the bio-based polymers, since Parkesine (considered the first plastic) and later celluloid are both obtained from cellulose. However, the cheaper alternative raw materials and new technologies that emerged, such as bakelite in 1907, provided the achievement of totally synthetic materials with their peak in the mid-1950s. Mainly because the plastic synthetic was more efficient in meeting the massive production of plastics required by the market. However, since the 1980s, bioplastics have become more interesting for society, due to the growing environmental awareness and the oil crisis of the 1970s, which alarmed the industry regarding its dependence on a finite and limited source (Lackner 2015).

The global production of bioplastics has increased steadily from the 1980s, reaching 2.11 million tons in 2019, and the production capacity is estimated to reach approximately 2.43 million in 2024. However, such a growth is still modest; the share of bioplastics in the market has not exceeded 1% of the more than 359 million tons of conventional plastics produced annually, and the growth can potentially increase due to the emergence of new products, applications of more sophisticated technologies, instability in the price of petrol, and demand of a group of consumers of greater environmental awareness (European Bioplastics and nova-Institute 2019; Imre and Pukanszky 2013; Imre et al. 2019).

### 8.3.4 Emerging Technologies for Bioplastics Produced with Hemicellulose

The concept of biorefinery can support the production of bioplastics by the industry, since a single raw material can yield several products of high value, and the integration of the various processes involved would reduce production costs (Lackner 2015). A good example is sugarcane, which, after being processed in a sugar and alcohol plant for the extraction of its sucrose used in alcoholic fermentation, results in bagasse, considered a by-product of low value. However, the considerable content of lignocellulosic molecules, such as hemicellulose, in the bagasse can potentially be applied for the bioplastics production (Brienzo et al. 2016). In other words, the addition of a structure and methods that can process such “wastes” and obtain important molecules to be applied in new products would guarantee a greater use of that initial raw material.

A higher implementation of biodegradable bioplastics by the industry requires the development of new technologies so that their production becomes feasible and competes with conventional plastics. Therefore, researchers have been looking for more resistant, inert, and biodegradable materials worldwide, which must also be easily deployed on an industrial scale.

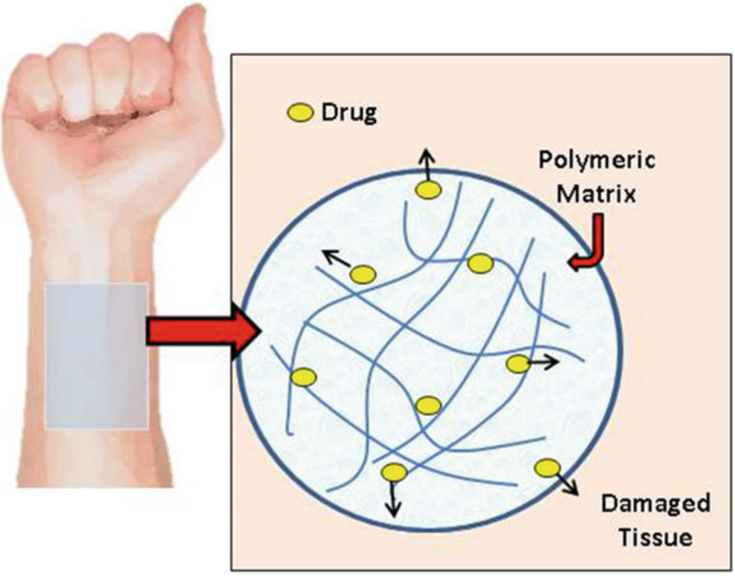

**Fig. 8.5** Drug-carrying biomaterial applied in tissue regeneration

Some plant polysaccharides are noteworthy for having several highly polar hydroxyl groups in their chains, with the potential to form strong intermolecular and intramolecular hydrogen bonds and provide, in some cases, considerable crystallinity to the macromolecular network. Due to its concentration in plant biomass, high availability (agro-industrial residues), biocompatibility, bioactivity, and biodegradation, hemicellulose can be employed in biotechnology, for the manufacture of biomaterials, (Brienzo et al. 2016; Cherubini 2010; Freitas et al. 2019; Gabrielli et al. 2000; Oliveira et al. 2010; Urtiga et al. 2020), with different applications (e.g., food packaging, tissue engineering, bio-devices, and drug delivery systems (Fig. 8.5) (Urtiga et al. 2020).

The challenges for the application of film based on hemicellulose are related to its heterogeneity, low mechanical properties, difficulty in forming continuous/homogeneous bioplastics, and hydrophilic property (Chen et al. 2016; Escalante et al. 2012; Goksu et al. 2007). Hydrophilicity, in particular, can provide structural benefits because the polar hydroxyl groups are able to form hydrogen bonds with other hydrophilic molecules, and these same molecules end up interacting with more water molecules from the ambient, making the film more sensitive to humidity.

Therefore, depending on the humidity and temperature conditions to which they are subjected, they can contain a large amount of water, leading to significant hydrolysis, decrease in mass, and instability in their properties during application (Imre et al. 2019). Based on these characteristics, hemicelluloses have good properties to be used in packaging for foods that do not interact with water like fatty foods (Naidu et al. 2018).

This chapter focuses on the manufacture of films since there is a recurring need to find a substitute for synthetic plastics used in packaging production. Hemicellulose has gain attention as a feedstock to film/biomaterial production. Materials based on biopolymers and biomolecules are an alternative to plastic films from non-renewable sources that persist in the environment. Such biomaterials have drawn attention mainly from the pharmaceutical industry, which sees them as promising drug-carrying systems, and from the food industry, which is the largest consumer of films for the packing of their products, representing 70% of the application of bioplastics (Naidu et al. 2018; Urtiga et al. 2020).

Regarding food, those packages must meet several safety and quality requirements, as to preserve the food and prevent any type of toxic contamination. The main function of packaging films is to protect products from external factors, such as effects of gases, water vapor, odors, microorganisms, dust, mechanical shocks, vibrations, and compressive forces; they can also serve as a vehicle for the incorporation of food additives (e.g., antioxidant, antimicrobial, flavoring and coloring agents) (Mikkonen and Tenkanen 2012; Tharanathan 2003).

Oxygen gas exerts a relevant impact on the properties of packaged food, changing the shelf life of a product. It can favor microbial growth, changes in color in fresh and cured meats, oxidation of lipids and consequent rancification, and senescence of fruits and vegetables, since compounds generated through an oxidative process can affect the texture, ability to store water, nutritional characteristics, and quality of food (Akram et al. 2019; Mikkonen and Tenkanen 2012). The presence of water or moisture should still be considered because the film must have good properties of barrier to water outlet and inlet since an increase in the water activity can generate chemical reactions, enzymatic changes, and microbial growth in the food (Mikkonen and Tenkanen 2012).

Bioplastics must meet those requirements to be accepted on the market. The composition and formulation of a biopolymer vary according to the raw material used. Agricultural products or residues can form combinations and be processed in the manufacture of polymers, which, with the addition of plasticizers or other additives, improve their capacity to form films with the desirable characteristics (Tharanathan 2003). However, Urtiga et al. (2020) claimed the ability of hemicelluloses (e.g., xylan) to form films is unsatisfactory due to the size of their chains, presence of branches, low molecular mass, relative high glass transition temperature, and low water solubility—unless they undergo heat treatment. In this sense, several procedures have been studied for overcoming those deficiencies, being the use of hemicelluloses in biodegradable films, as well as in composite films, a good alternative. Therefore, modifications in the different types of hemicellulose (chemical, enzymatic, and cross-linked ones) and/or addition of other polymers and fillers to the polymeric matrix are an alternative for obtaining bioplastics with better properties and characteristics for different applications (Urtiga et al. 2020).The response of the different methods used is influenced by the characteristics of each hemicellulose. Due to the heterogeneity of the polysaccharide, its use depends on its degree and type of substitution, degree of polymerization, and extraction process (Urtiga et al. 2020).

Using xylan extracted from sugarcane bagasse, Jin et al. (2019) analyzed the effect of molecules of different molecular weights (8200–26,800) and different amounts of lignin (1.6–9.5%) and observed hemicelluloses of higher molecular weight and low number of branches and lignin content provided films with better mechanical properties. Lignin in films with hemicellulose of low molecular mass acted as a reinforcing agent for the polysaccharide; however, it might be an impurity in hemicellulose of high molecular weight, thus impairing the mechanical properties of the film. Using xylan extracted from cotton stalk and birchwood, Goksu et al. (2007) corroborated the possibility of lignin promoting the formation of films based on xylan, because when lignin was present with at least 1% (w/w) it acted as a plasticizer in these films.

### 8.3.4.1 Importance of Plasticizer for Hemicellulose Films

The addition of plasticizers to films produced with biomolecules aims to increase the plasticity of the material, altering its ability to change shape, through changes in rheological and mechanical properties (Bertuzzi et al. 2012; Imre and Pukanszky 2013). Plasticization improves flexibility and elongation, enabling the film to undergo greater deformation until it reaches the breaking point. However, the addition of a plasticizer in the composition of a film can reduce its mechanical strength (Bertuzzi et al. 2012; Xu et al. 2019). The mechanical properties of films are strongly influenced by the plasticizer's nature and its concentration (Imre and Pukanszky 2013; Li and Huneault 2011).

Many biomolecules (e.g., polysaccharides) have low deformability and resistance to impact due to the conformation of their chains, which have limited mobility. The use of plasticizers reverses this situation, since they can weaken the hydrogen bonds between the polymer chains and increase the free volume and chain mobility, as illustrated in Fig. 8.6, changing some of the film's properties (Imre and Pukanszky 2013; Xu et al. 2019).

Bertuzzi et al. (2012), Imre and Pukanszky (2013), Li and Huneault (2011), and Xu et al. (2019) addressed the use of polar molecules or compounds of relatively low molecular mass in the plasticization of films (e.g., water, glycerol, sorbitol, propylene glycol, urea, and formamide). Although water has proven an efficient plasticizer, the use of compounds of higher boiling point, such as glycerol, is often preferred, since they decrease sensitivity to water and make some of their properties more stable (Imre and Pukanszky 2013; Li and Huneault 2011).

A comparison of the effects of two plasticizers (sorbitol and glycerol) on films based on arabinoxylan revealed the plasticizers proportion can lead to different consequences in the mechanical properties of the films. Films with concentration of 10% (w/w) in glycerol resulted in higher tensile strength than those containing 10% of sorbitol. However, the films exhibited an opposite behavior when the plasticizers concentration was 40% (w/w), the film with sorbitol was more resistant. Although the presence of 10% of sorbitol has resulted in films with low tensile strength, these films showed lower water vapor permeability, 1.1 g mm/ ($m^2$ d kPa) (at a relative humidity gradient of 0–54%) while the corresponding films with glycerol showed permeability value equal to 3.3 g mm/ ($m^2$ d kPa). Films containing

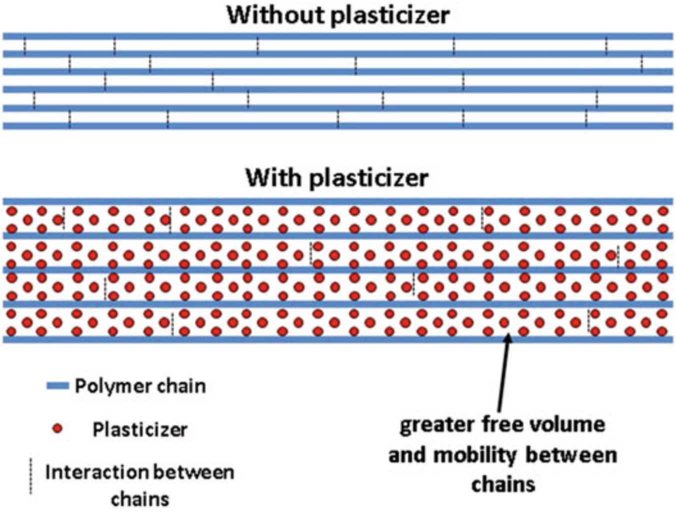

**Fig. 8.6** Presence of plasticizer in polymers

10% (w/w) of glycerol or sorbitol showed similar values of oxygen permeability of 3 $cm^3 \mu m/(m^2$ d kPa) at 50–75% of relative humidity. However, when the plasticizer concentration was 40%, the films with sorbitol proved a better barrier to oxygen than glycerol (7.4 and 4.7 $cm^3 \mu m/(m^2$ d kPa, respectively). In both cases, the increase in the plasticizer content increased the permeability of the films to water and oxygen (Mikkonen et al. 2009).

Xu et al. (2019) compared the influence of three different plasticizers, namely glycerol, xylitol, and sorbitol on the composition of films based on hemicellulose and chitin reinforced with cellulose nanofibers. The authors observed a 10 to 40% variation in the plasticizer concentration slightly increased the water vapor permeability, oxygen permeability, transparency, solubility, and low contact angle of the plasticized films, in comparison to non-plasticized ones. Among the plasticizers studied, glycerol generated a greater tension in the break (7.8–18.53%), while the films in which sorbitol was used showed higher tensile strength (23.14–48.96 MPa).

An often overlooked problem is the tendency of some plasticizer compounds to migrate to the surface of the products, altering the macroscopic properties of the biofilm. In this way, plasticizer can diffuse out of material causing environmental and health problems depending on the released concentration (Imre and Pukanszky 2013). To minimize this effect, plasticizers with higher molecular weight are generally used, as they diffuse more slowly, and as a result the migration rate of the plasticizer to out of the material is reduced. However, such an application decreases the efficiency of the plasticizer in increasing the mobility of polymer chains (Bertuzzi et al. 2012; Imre and Pukanszky 2013).

#### 8.3.4.2 Development of Biomolecule Blends

Films are usually produced with the addition of different compounds, forming blends, or composites, whose performance is dependent on the control of the structure and the interfacial adhesion, for facilitating the transfer of tension among the different phases of the material. An alternative to reduce hydrophilicity in some vegetable polysaccharides would be to mix them with a more hydrophobic matrix (Imre et al. 2019).

Examples of polymers good for blending are proteins and polysaccharides, like cellulose. Cellulose is a natural resource highly available, has hydrophobic character, chemical compatibility with other polysaccharides, crystallinity, and has been used to improve mechanical, thermal resistance, and water vapor barrier properties of bioplastics (Hansen et al. 2012). However, the dimensions and amount of cellulose in bioplastics are important factors, since cellulose can be used with different dimensions and high concentrations can generate fiber agglomerations, thus, reducing the properties of bioplastics (Chen et al. 2009a, b; Do Lago et al. 2020; Guimarães et al. 2016; Xie et al. 2014). Several studies have confirmed the improvement in the properties of hemicellulose-based bioplastics with the addition of cellulose nanofibers (Azeredo et al. 2010; Gordobil et al. 2014; Long et al. 2019; Lopez-Rubio et al. 2007; Mikkonen et al. 2011, 2012; Plackett et al. 2010; Stevanic et al. 2011; Svagan et al. 2007, 2008). Peng et al. (2011) observed nanocellulose reinforcement promoted mechanical resistance in films composed of hemicellulose (xylan). In bioplastics made with 5, 10, 15, and 20% (w/t) nanocellulose, both tensile strength properties (15.5, 20.2, 28.9, and 39.5 MPa, successively) and Young's modulus (1322, 1578, 2355, and 3404 MPa, successively) increased, thus reducing elongation (2.9, 2.6, 1.8, 1.4%, successively). The authors also reported an increase in the thermal stability of xylan-based bioplastics with the addition of nanocellulose. Such an improvement and the mechanical properties may be related to the linear and homogeneous structure of cellulose, optimization of hydrogen bonds (high aspect ratio), and increased crystallinity of bioplastics with nanocellulose. The addition of nanocellulose to xylan-based bioplastics can also increase barrier properties (reduced water vapor and oxygen permeability) (Hansen et al. 2012) due to the formation of tortuous paths of nanofibers in the bioplastic matrix, hampering the passage of water vapor through the bioplastic (Saxena et al. 2011).

Chitosan is another promising compound for application in films with hemicellulose due to its various hydroxyl and amine groups capable of forming hydrogen bonds with hemicellulose (Fig. 8.7), showing good miscibility between the two polysaccharides (Xu et al. 2019). Investigating the gel-forming capacity of films made with chitosan and xylan with the use of FTIR, Gabrielli and Gatenholm (1998) observed possible interactions between the functional glucuronic acids of xylan and the amino groups of chitosan, and suggested the formation of a three-dimensional network. The proportion of those polysaccharides can affect their miscibility. Dynamic mechanical and a microscopic atomic force analyses revealed films homogeneous composed of 10% chitosan and 90% hemicellulose, however, when was employed 70% of chitosan and 30% of hemicellulose, a two phases system was identified.

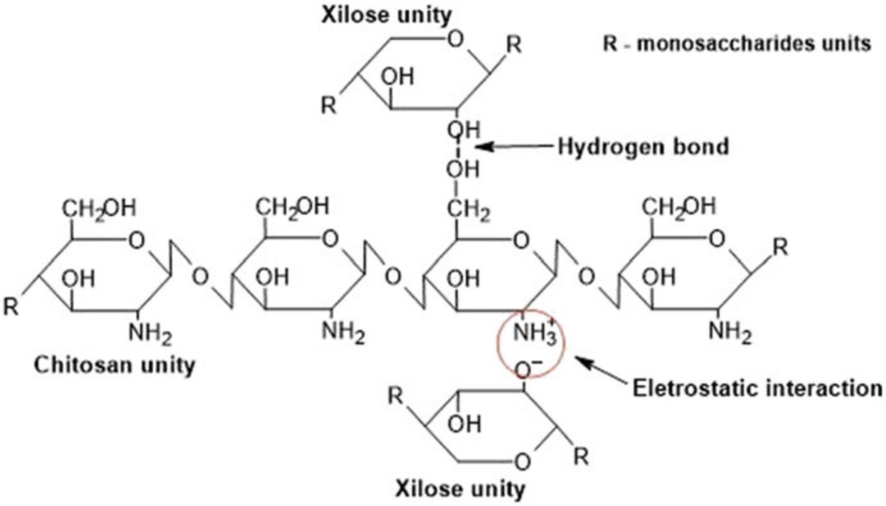

**Fig. 8.7** Interaction between chitosan and xylan

Arabinoxylan (AX) and arabinoxylooligosaccharides (AXOS) of different molecular masses were combined to produce edible films based on chitosan (Costa et al. 2015). Films composed of high molecular mass AXs (3670 and 3503 degrees of polymerization) slightly improved the mechanical properties of chitosan-based films. The authors concluded films could be made with those constituents due to the prebiotic benefits of XOS.

The reinforcement with nanofibers of cellulose also substantially improved the tensile strength of films composed of hemicellulose and chitosan. With no reinforcement, the tensile strength of the films was 16.24 MPa with the addition of 5 to 20% cellulose (based on the dry weight of chitosan and hemicelluloses), and the tensile strength increased to 53.75 and 69.16 MPa, respectively (Xu et al. 2019).

The correlation between hemicellulose and chitosan can still provide some benefits for food preservation (Li et al. 2011). Products from the Maillard reaction, which occurs between an amino group and reducing sugar aldehydes or ketones exposed to high temperature, can show excellent antioxidant and antimicrobial activity. This was evidenced in this study, which used chitosan (rich in amino groups) and xylan (source of reducing sugars). The latter is composed of xylose, which has high reactivity, thus increasing the reaction speed and showing promising in obtaining complexes with antioxidant and antimicrobial properties (Shibao and Bastos 2011).

#### 8.3.4.2.1 Compatibility and Miscibility

In some cases, the blend components do not interact well. In such cases, a series of chemical and physical modifications can improve the integration among different materials, making them more compatible. Although compatibility and miscibility are not completely independent terms, they are often confused. Miscibility describes the number and composition of phases in a mixture of polymers and is determined by a thermodynamic factor called enthalpy free from the mixture as showed in Eq. (8.1) (Imre et al. 2019).

$$\Delta G_{\text{mix}} = \Delta H_{\text{mix}} - T\,\Delta S_{\text{mix}} \tag{8.1}$$

where, $\Delta G$, $\Delta H$, $T$, and $\Delta S$ represent variation in free enthalpy, variation in enthalpy, temperature, and variation in entropy, successively. When blends are formed by components of high molar mass, the contribution of entropy becomes highly negligible, and the resulting morphology is determined by enthalpy (Imre et al. 2019). If this factor is negative, the mixture is homogeneous and, therefore, shows no formation of separate phases. The free enthalpy of a mixture is correlated with the intramolecular and intermolecular interactions between the compounds of the mixture. A completely miscible mixture is rarely found, due to the lack of some specific interactions. Therefore, in practice, most constituent pairs of a mixture are at most partially miscible, containing two different phases with an abundance of a certain constituent and a small fraction of another (Imre et al. 2019).

Compatibility is a technical term that refers to the property profile of a mixture in relation to its mechanical characteristics, processability, transparency, permeability, surface quality, or degradability. The degree of compatibility of a mixture can be measured, for example, by the relative tensile strength. In this case, blends with greater miscibility will show higher resistance, differently from blends based on immiscible compounds which, due to their more complex morphology, undergo consequent micromechanical deformation processes. Compatibility is generally given as a function of interfacial adhesion between two or more phases, which is dependent on the strength and number of interactions, often determined by the chemical structure of macromolecular chains (Imre et al. 2019).

The most common compatibility techniques involve the addition of additives that will act at the interface of the constituents of the mixture, promoting adhesion between them. In this case, non-reactive compatibilization occurs (a compatibilizing agent is used and characterized by an amphiphilic compound). Its structure usually has a copolymer block prefabricated and inserted in the blend, which has a polar portion and a nonpolar one. The other possibility in this technique is reactive compatibilization, in which an amphiphilic structure is formed in situ during mixing. Reactive compounds of low molar mass are normally used and act as coupling agents forming covalent bonds between the phases. Reactive methods are generally more efficient, especially in polysaccharides such as hemicellulose, since they show several hydroxyl groups that can potentially undergo reactive modifications. Numerous bifunctional compounds can form covalent bonds with polysaccharides (e.g., organic bi and trifunctional acids, malic and succinic anhydride, and silane and diisocyanate compounds). Several studies have reported promising results on the use of citric, malic, and tartaric acids, which are more environmentally appropriate, non-toxic, and non-volatile alternatives. Moreover,

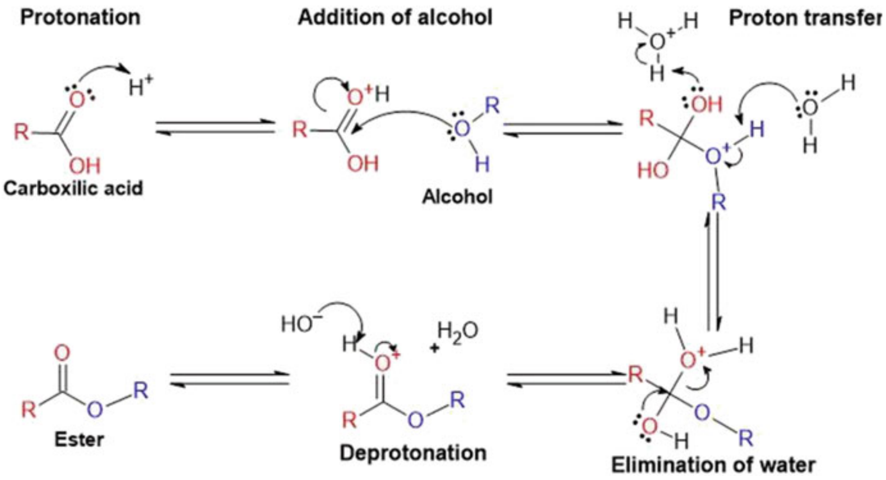

**Fig. 8.8** Esterification reaction

they are abundant and relatively more accessible, since they are obtained from inexpensive biological routes (Imre et al. 2019).

Chemical modifications can not only guarantee better crystallinity and compatibility among hemicellulose and other components of a mixture, but also make the film/biomaterial more hydrophobic (Cunha and Gandini 2010; Gordobil et al. 2014; Soderqvist-Lindblad and Albertsson 2004). Such reactions aim to replace the hydroxyl group with a hydrophobic one. Therefore, an increase in its hydrophobicity improves the water-resistance of the films, their thermal stability, thermoplastic properties, and solubility in organic solvents (Farhat et al. 2016). Reactive methods commonly used are esterification, etherification, or oxidation.

Esterification involves the reaction between an alcohol and a carboxylic acid towards forming an ester, conventionally with the use of anhydride or acyl chloride as esterifying reagents (Fig. 8.8) (Imre et al. 2019; Zhang et al. 2020b). Several esterification processes, such as acetylation, propionylation, and oleylation, have been adopted for the generation of hydrophobicity in hemicellulose (Farhat et al. 2016). Acetylation is a chemical modification that links an acetyl group to the hemicellulose chain. When conducted prior to film formation, this process reduces water solubility and increases its thermal stability, also improving its mechanical properties such as flexibility, and its hydrophobicity, which is essential for maintaining the barrier property of packaging based on hemicellulose under high humidity (Stepan et al. 2012; Ayoub et al. 2013; Gordobil et al. 2014; Gröndahl et al. 2003).

However, some of such esterification processes tend to form by-products from the severe acidic degradation of hemicellulose. Therefore, processes based on transesterification with vinyl ester can be an alternative to a milder acylation method, avoiding the formation of decomposition products. Zhang et al. (2020b) studied the transesterification process using vinyl laurate to chemically modify hemicellulose

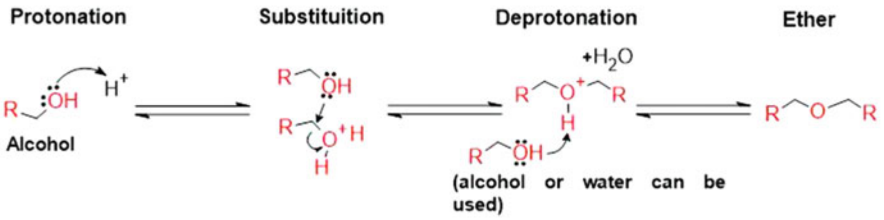

**Fig. 8.9** Etherification reaction

and evaluate the films produced. The films showed an approximately 120° water contact angle, hence, excellent hydrophobicity and improved mechanical properties, like tensile strength (33.94 ± 3.09 MPa) and elongation at break (22.41 ± 2.87%). Moreover, the modified hemicellulose films showed a good barrier to water and oxygen, with permeability values ranging from 1.59 ± 0.07 to 2.23 ± 0.11 ($10^{-10}$ g/m s Pa) and 1.21 ± 0.04 to 4.24 ± 0.30 ($\mathrm{cm}^3 \mu\mathrm{m}/\mathrm{m}^2$ d kPa), respectively.

Hemicellulose can also be altered by etherification, which consists of a reaction between an alcohol and an alkylating agent, such as alkyl halides (chlorides, bromides, and iodides), alkyl sulfonates, vinyl monomers, and epoxides (Fig. 8.9). Carboxymethylation is an example of etherification and involves the reaction between hemicellulose and sodium monochloroacetate in alkaline conditions. Such modifications can potentially improve the thermal stability of the formed films and reduce their hydrophilicity (Ren et al. 2008). Benzylation, a type of etherification, also replaces the hydrogen atoms of the hydroxyl group with benzyl groups, in a reaction with benzyl chloride (Sereshti and Mohammadi-Rovshandeh 2003). Such a process increases the hydrophobicity of the film as well as its oxygen barrier and thermal stability (Hartman et al. 2006; Ren et al. 2012).

Fluorination is a process that can be applied after the formation of hemicellulose-based films, in a reaction, for example, with trifluoroacetic anhydride. It provides unique chemical and surface properties such as high hydrophobicity, chemical resistance, and thermal stability. Films that undergo fluorination have a strong barrier to gases and liquids, a low friction coefficient, and low humidity (Farhat et al. 2016; Gröndahl et al. 2006; Tressaud et al. 2007; Woodward et al. 2003).

Oxidation, another reactive approach, is based on redox reactions between the -OH groups of polysaccharides and ions (Fig. 8.10). Using this method, Kochumalayil et al. (2013) chemically modified xyloglucan towards reducing its glass transition temperature, so that it became more malleable and moldable from a milder heat treatment. Periodate ion oxidized the hydroxyl groups present in xyloglucan, resulting in the breaking of the xylose ring and formation of dialdehyde groups, which were subsequently modified through a reduction reaction with sodium borohydride in alcohols, as well as perturbations in the packing of modified xyloglucan chains, changes in intermolecular interactions, and increased molecular mobility.

**Fig. 8.10** Oxidation reaction

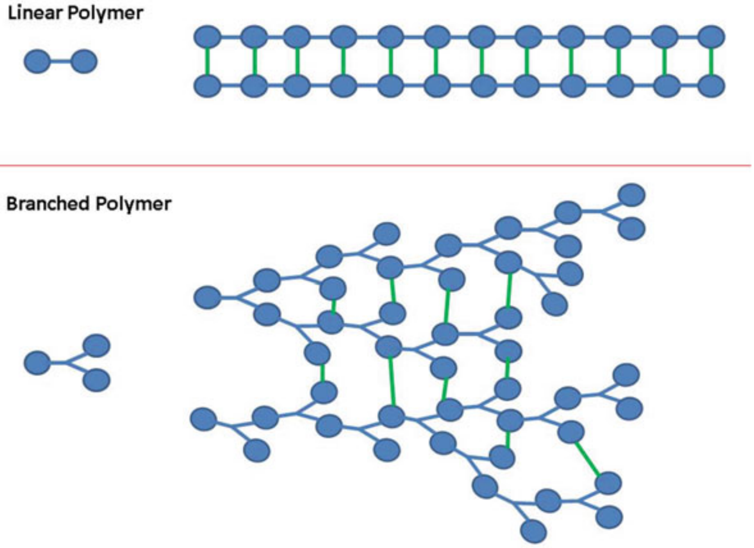

**Fig. 8.11** Chains cross-linked

### 8.3.4.3 Crosslinking Agents in Polymeric Chains

Crosslinking agents are additives that act on one or more phases of the polymer providing cross-links between its chains (Fig. 8.11). Such a process increases the barrier to oxygen and water vapor, the hydrophobicity of the formed films, (Azeredo et al. 2015; Zoldners and Kiseleva 2013), their tensile strength and elongation, as well as other properties such as transparency and surface homogeneity (Guan et al. 2016; Shao et al. 2019).

Crosslinking generally involves the reaction between a polysaccharide and a carboxylic acid (e.g., oxalic acid, citric acid, or succinic acid) and can be influenced by both cross-linker content and reaction temperature (Chen et al. 2015; Guan et al. 2016; Mikkonen et al. 2013). Ammonium zirconium carbonate (AZC) is a cross-linker effectively evaluated in different hemicellulose-based films to improve their mechanical resistance (Chen et al. 2015). The use of epichlorohydrin has also been studied in films made of quarternized hemicellulose and chitosan, which display a uniform porous structure, good optical transparency, and excellent mechanical resistance (Guan et al. 2016). However, epichlorohydrin shows carcinogenic potential (U. S. Department of Health and Human Services 2016), therefore, its application and proportion are limited in the production of biodegradable plastics.

Some acids (e.g., citric acid) act as both a crosslinking agent, due to di-ester intermolecular bonds between the hydroxyl groups of the polysaccharide with two of its carboxylic groups, and a plasticizer, as reported by Shi et al. (2008). However, their quantity must be moderate, since their excess can lead to a thermosetting behavior of the material.

#### 8.3.4.4 Functional Biopackages

Several studies have focused on the development of functional bioplastics for use as food packaging that can change the conditions of the packaged product, improving its quality, increasing its life span, safety for consumption, and sensory properties, and providing a better nutritional value. Among such technologies, those aiming at preventing contamination or oxidation processes in packaged foods through active compounds have excelled (Coma 2013; Medina-Jaramillo et al. 2017; Valdés et al. 2014). The active compounds may be too volatile to be applied directly to the food; therefore, an advantage of functional biopackages is their potential for a controlled release of those active agents, ensuring the quality of the food for longer time (Coma 2013; Valdés et al. 2014). Moreover, the slower release of the agents prevents their concentration beyond the limit allowable in food (Mugwagwa and Chimphango 2020).

The use of antimicrobial substances in packaging is intended to solve problems of contamination in food, since they inhibit the growth or even cause the death of pathogenic and/or deteriorating microorganisms. However, one of the great challenges for their application is to find the limit between their resistance to the attack of microorganisms during their useful life and their degradation at the end of their cycle (Coma 2013; Valdés et al. 2014). Essential oils, organic acids, nisin, chitosan, microparticles, and nanoparticles (silver, gold, copper, titanium dioxide, magnesium oxide, calcium oxide, and zinc oxide) can be used for this purpose. The latter compounds interact with the bacterial cell wall destroying its integrity. The use of titanium dioxide ($TiO_2$) in functional films not only improves their mechanical properties, but also shows antibacterial performance in functional chitosan-based films incorporated with hemicelluloses (Zhang et al. 2020a). However, inorganic additives are not biodegradable and slow down the biodegradation of the material when exposed to the environment (Campos et al. 2010; Capelezzo et al. 2018; Silva et al. 2014).

Several studies have focused on natural extracts from plants, essential oils, or agricultural residues. The antimicrobial and antioxidant capabilities of, for example, extracts of grape seed, green tea, raspberry, among other natural products that have relevant compounds for such an application (e.g., low molecular weight phenolic acids, tannins, proanthocyanidins, flavonoids, and others) are known (Valdés et al. 2014).

Mango peel polyphenol extract was incorporate into acetylated hemicellulose-nanocellulose films coated with polycaprolactone. The films were immersed in polyphenol extract for 1 min, and the amount of the mango polyphenols absorbed was 2.89 mg/g Gallic acid equivalent. The antioxidant activity of polyphenol extract was efficient in packaging food, because it increased temperature and time, hence, their release into the food. The greatest release of antioxidants occurred in fatty foods, since mango polyphenolics are recognized as hydrophobic (Mugwagwa and Chimphango 2020).

Essential oils can be easily incorporated into aqueous polymeric solutions for the obtaining of film. In general, they reduce water permeability, often due to its hydrophobicity, since the impact of lipid on the microstructure of emulsified films is a determining factor regarding efficiency as a water barrier. In turn, such microstructures are affected by other factors (e.g., physical state of the oil and its distribution in the polymer). However, they can also affect the structural, physical, and bioactive properties of the biofilm, thus triggering discontinuity in the polymeric network. The use of essential oils is more limited to the formation of films by casting, which hinders their application in the industry, which prefers compression molding or extrusion, in which high temperature is applied to the material (Atarés and Chiralt 2016).

The use of linoleic acid in films made from carboxymethylated-xylan resulted in films of weaker mechanical properties, probably due to the presence of a large number of hollow regions and thickness. However, such films showed less permeability to water vapor and oxygen, and antimicrobial activity against gram-positive bacteria (Queirós et al. 2017). The outer membrane of gram-negative bacteria may explain the low susceptibility of such microorganisms to the action of lipidic antimicrobial agents, which limits the diffusion of hydrophobic compounds through the lipopolysaccharide membrane. The antimicrobial activity of fatty acids is related to the size of the aliphatic chain and number of double bonds so that long unsaturated chains tend to be more effective against gram-positive bacteria than gram-negative ones (Akram et al. 2019; Queirós et al. 2017). Antioxidant and antibacterial properties of licorice essential oil into carboxymethyl-xylan films were evaluate, even after being stored for 20 days at 25 °C. Discs of the films (10 mm diameter) were placed on the surface of seeded agar plates and showed antibacterial activity against two recognized foodborne pathogens, namely *Enterococcus faecalis* and *Listeria monocytogenes* (both Gram-positive), of 8.53 and 17.31 mm inhibition zones diameters, respectively. The antioxidant activity inhibited approximately 20% of free radicals after 5 h. Moreover, films with essential oils significantly inhibited lipid peroxidation, unlike the control films (Luís et al. 2019).

Phenolic and terpenoid compounds are generally responsible for the antimicrobial activity of essential oils. Oregano and thyme exert an effective action against the development of gram-negative and potentially pathogenic bacteria such as *E. coli* and several Salmonella subspecies, due to phenolic components (e.g., thymol and carvacrol) in their composition (Akram et al. 2019). Apart from the antibacterial effect, some of those essential oils display antioxidant properties, limiting lipid peroxidation by decreasing the formation of free radicals or sequestering them. They can neutralize them using chelating transition metals capable of extinguishing oxygen singlets and triplets from the decomposition of peroxides. Lately, there is a greater interest in natural antioxidants, due to consumer preference and possible toxicity of synthetics (Akram et al. 2019).

Although essential oils are registered as safe food additives, they can cause some allergic reactions and dermatitis (e.g., orange, lemon, and Litseacubeba oils provoke phytotoxic reactions after frequent use). The Information Network of Departments of Dermatology (IVDK) is a multicentric project founded in 1988, comprised of more than 50 skin clinics in Germany, which record and develop scientific analyses of contact allergies. Between 2000 and 2008, it registered 637 cases of hypersensitivity caused by oils of ylang-ylang, lemongrass, jasmine, sandalwood, and cloves. The use of essential oils in the composition of biofilms can promote several beneficial characteristics; however, depending on the application, attention must be paid to the more than 80 oils registered as causing contact allergies (Akram et al. 2019).

Naturally, hemicellulose is not an antioxidant, but chemical modifications can give it such a property. When modified by transesterification with vinyl laurate, hemicelluloses showed an improved antioxidant activity (reaching a radical scavenging activity of approximately 38%), due to the introduction of laurate chains in its hydroxyl groups (Zhang et al. 2020b). Moreover, the effect of the combination of hemicellulose and chitosan during the Maillard reaction generated products with antioxidant activities (Li et al. 2011).

Smart packaging has also drawn the attention of researchers, since this system performs functions that enable the detection of deterioration processes and temperature fluctuations during storage, and indicate whether a fruit is ripe, providing information and alerts on the quality of packaged products. This technology also seeks natural compounds that can fulfill this function, since synthetics can have relatively greater toxic and mutagenic potential. Such composites can be found in vegetables, fruits, grains, herbs, and flowers (Bhargava et al. 2020; Medina-Jaramillo et al. 2017; Vedove et al. 2021).

Food contamination and deterioration are usually related to pH modification. Natural pigments, like chlorophyll and carotenoids, can be found in several natural extracts and change color when exposed to changes in pH. For example, when incorporated in a film-forming starch matrix, extracts of green tea and basil can improve their mechanical properties, impermeability to water vapor, and antioxidant activity. Moreover, they are stable at high temperatures, resisting those above 240 °C without degrading. However, the presence of natural pigments makes them suitable for applications in smart packaging (Medina-Jaramillo et al. 2017).

Anthocyanin from grape is a natural pigment that can be incorporated into bioplastics. Food spoilage processes release ammonia, lowering pH and changing the color of anthocyanin from purple to blue. However, the major obstacle for the industrial application of this material is its thermal stability (Vedove et al. 2021).

Several studies have focused on other natural compounds such as curcumin, tannins, betalain, quercetin, baseline, and their application as indicators of other properties (e.g., temperature change, an essential factor that can affect both safety and quality of food). Those indicators provide such information through a continuous, clear, and irreversible reaction in response to temperature changes. The duration of their exposure to temperature variations is represented by variations in color and corresponds to the stability of the food product stored. Sensitivity to the levels of $CO_2$ and $O_2$ is also used in evaluations of the quality of packaged products, since carbon dioxide is generated during the metabolism of microorganisms, and when $CO_2$ is exposed to sensors based on luminescent pigments the package emit fluorescence (Bhargava et al. 2020).

#### 8.3.4.5 Other Applications of Hemicellulose as a Biomaterial

Hemicellulose has attracted attention and been studied in the area of food packaging. However, this biomolecule can also potentially form hydrogels, which are polymeric networks with cross-links that absorb large amounts of water without losing their structure. Such an ability to retain water is similar to that of living tissues, thus making hydrogels suitable for biomedical applications (e.g., drug distribution) (Naidu et al. 2018; Urtiga et al. 2020).

Hydrogels based on polysaccharides such as hemicellulose have been developed for different purposes apart from drug distribution (e.g., as cell immobilizing matrix and in tissue engineering). Hemicelluloses are not toxic, and are biocompatible, biodegradable, widely available from renewable sources, and display a variety of promising structures for the production of macromolecular networks (Naidu et al. 2018; Urtiga et al. 2020). Urtiga et al. (2020) proposed the use of xylan-based hydrogel as a controlled distributor of medicines in the colon region, since this polysaccharide is not digested by the human gastrointestinal system, but can be degraded by bacteria present in a certain region of the intestines. Such hydrogels are obtained mainly by inducing physical or chemical reticular reactions, for example, they can be produced through chemical crosslinking and the use of horseradish peroxidase and hydrogen peroxidase enzymes as catalysts. Hydrogel loaded with caffeine demonstrated efficient diffusion in both distilled water and 0.1 mol/L HCl solution (Iravani et al. 2011). Sun et al. (2013) used xylan from wheat straw for the production of hydrogel with acrylic acid and N,-N-methylene-bisacrylamide as cross-linkers, and observed the release of compounds was influenced by pH—the greater release had duration of 5–6 h with a pH of 7.4.

As in film production, the development of hydrogels with xylan can consider adding other compounds. Regarding synthetic compounds, the composition with acrylic derivatives is the most common. Xylan hydrogels were mixed with N-isopropylacrylamide and acrylic acid, and with methacrylate acid (Gao et al. 2016; Sun et al. 2015). However, hydrogels with other functionalities can also be obtained (e.g., a photosensitive hydrogel based on xylan with azobenzene as a copolymer for the selective release of vitamin $B_{12}$ promoted a better release at neutral pH and with UV irradiation (Cao et al. 2014).

The use of blends with synthetic polymers can eventually incur risks, since the literature has reported some cytotoxicity. Such negative aspects can be related to their molecular mass, electrical charge (cationic polymers are generally more toxic than anionic ones), ramifications, concentration, and exposure time (Urtiga et al. 2020). Hydrogels can also be manufactured from only natural macromolecules such as chitosan associated with xylan (Gabrielli and Gatenholm 1998; Gabrielli et al. 2000). Another approach is the use of blends with natural and synthetic molecules (e.g., Kappa-carrageenan followed by mixing with polyvinyl-pyrrolidone associated with xylan of different origins) (Meena et al. 2013).

Xylan-based hydrogels can be employed in several applications, including tissue regeneration. Tests performed on rats with bone problems revealed hydrogels with xylan improved the recovery rate compared to those with only chitosan (Bush et al. 2016), and was reported their potential for application in the remediation of water-absorbing heavy metals (Peng et al. 2012). In the present study, xylan was combined with acrylic acid—859 mg, 495 mg, and 274 mg of palladium, cadmium, and zinc, successively, were removed for each hydrogel gram. Moreover, a subsequent easy hydrogel regeneration and metal recovery were obtained. Another interesting approach is the obtain of magnetic hydrogel through the addition of acrylic acid and $Fe_3O_4$ to hydrogel based on xylan. Tests with blue methylene showed the hydrogels presented a maximum value of absorption equal to 438.6 mg/g of hydrogel (Sun et al. 2015). Still using magnetic $Fe_3O_4$, acetylated xylan hydrogel was synthesized to detect hydrogen peroxide. The produced hydrogel showed peroxide sensitivity to a concentration of 5μmol/L (Dai et al. 2016).

Xylan hydrogel can immobilize microorganisms and enzymes (e.g., *Propionibacterium acidipropionici)* to produce propionic acid via fermentation (Wallenius et al. 2015). Lipase was also immobilized showing more tolerance to higher pH and temperature than when it was free (Park et al. 2015). The properties of hemicellulose also enable its use as an wood adhesive, although little research has been developed in this area (Norström et al. 2015). Adhesives must wet, drain and penetrate the surface of the wood obeying a limit for an adequate adhesion. Hemicellulose can be used as adhesive altering their properties by adding of xylan dispersing agents such as polyvinyl-alcohol or polyvinyl-amine, and cross-linkers such as glyoxal or hexamethyl-oxymethyl melamine.

## 8.4 Concluding Remarks

Environmental pollution caused by plastics has affected life in different biomes and can potentially impact human health. Over the past few decades, it has been a matter of concern for many countries. However, since the number of plastic residues found in nature is significant, the measures adopted may have been unsatisfactory. At least part of the traditional plastics must be replaced with a biodegradable version preferably from renewable sources. Hemicellulose biomolecule is a good example for such an application, since it is abundant in nature and has numerous hydroxyl groups capable of making hydrogen bonds. Hemicellulose is biocompatible with other biomolecules, and studies have shown its efficiency as a barrier to oxygen and its promising antioxidant effect when complexed to certain protein molecules. However, some challenges must be overcome so that the hemicellulose based-material can be more suitable for film formation. Depending on the desired application, the hemicellulose hydrophobicity must be modified. Solutions are based on chemical modifications of hemicellulose, addition of additives such as plasticizers and cross-linkers, formation of bio-composites with other polymers, among other procedures that improve its miscibility in polymeric matrices, mechanical resistance, and action of water. Hemicellulose-based materials can meet the requirements of industrial large-scale production through the functionalization of their structure. From the first versions of the plastics used by the industry (biobased-ones) to the various types currently used (mostly synthetic ones), profit and financial losses have dictated the industry's preference for the material to be implemented. However, consumers' increasing awareness is a new factor to be considered, since such consumers desire products that do no harm the environment. In this sense, bioplastics have become more attractive to the industry as more sustainable alternatives of viable production.

**Acknowledgments** The authors acknowledge the São Paulo Research Foundation (FAPESP) for the financial support (process number 2019/12997-6; and 2017/22401-8) and the National Council for Scientific and Technological Development (CNPq) for the scholarship granted (process number 130499/2019-6).

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# Oligosaccharides from Lignocellulosic Biomass and Their Biological and Physicochemical Properties

# 9

Caroline de Freitas, Cárol Cabral Terrone, Carolina Froes Forsan, Adriane M. F. Milagres, and Michel Brienzo

## Abstract

Hemicellulose present in lignocellulosic biomass can be converted into higher value-added products such as xylooligosaccharides and mannan oligosaccharides. These oligosaccharides have physicochemical and biological properties of great interest to several industry sectors, which has made them emerging molecules. They can be produced through chemical or enzymatic hydrolysis, focusing on high efficiency and income to fulfill market needs. The most well-known characteristic of these oligosaccharides is their action as prebiotics, since they are not digested by the human digestive system and can be used by the intestinal flora; however they present several other health benefits and technological uses. Nowadays, besides industrial production, research on novel production strategies is increasing, since these oligosaccharides have several advantageous properties and can be produced from a low-cost substrate.

## Keywords

Lignocellulose · Hemicellulose · Oligosaccharides · Xylooligosaccharides · Prebiotics

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## 9.1 Introduction

The concept of biorefining is aligned with the search for new products through sustainable processes. The lignocellulosic biomass, being composed of three main classes of polymers (cellulose, hemicellulose, and lignin), can be converted into a wide spectrum of compounds (Ajao et al. 2018). The commercial potential of hemicellulose is large; however, it can be improved with the evolution of production processes. For this reason, many types of research are being carried out in recent years to explore hemicellulose from biomass for use in various industrial sectors, such as fuel, food, pharmaceutical, and cosmetics (Naidu et al. 2018; Ahmad and Zakaria 2019).

Due to increased public awareness of the role of food in promoting human health, consumers have preferred foods with additional attributes beyond their nutritional properties. Thus, scientific research has also begun to investigate the biological activity of food in human health. In the context of functional foods, biocomponents added to foods as supplements, prebiotics is promising ones. Many fermentable carbohydrates have been reported to have prebiotic effects, but the most widely documented prebiotics to cause human health benefits are non-digestible oligosaccharides (Singh et al. 2015).

Xylooligosaccharides (XOS), mannan oligosaccharides (MOS), and arabinooligosaccharides (AOS) are non-digestible oligosaccharides (NDOs) that can be obtained by hemicellulose bioconversion through chemical and/or biological processes, including pretreatments and fermentation (Mussatto and Mancilha 2007). These oligosaccharides are water-soluble, usually composed of 3–10 monosaccharides and considered as food components with prebiotic properties, due to their selective potential to stimulate the growth of beneficial microorganisms in the intestinal tract (Sophonputtanaphoca et al. 2018).

XOS and MOS are compounds that have β-linkages in their structure, which are resistant to hydrolysis by human digestive enzymes. Therefore, they reach the intestinal tract intact and can be used by the intestinal flora. XOS and MOS fermentation by gut bacteria produce short-chain fatty acids (SCFA) such as acetate, propionate, and butyrate that are related to the improvement of several intestinal functions, such as absorption of minerals and regulation of lipid and glucose metabolism (Singh et al. 2015). In addition, the growth of beneficial bacteria is favored by the consumption of prebiotics, making it difficult for pathogenic bacteria to establish, which in turn helps to prevent infections and allergies (Farias et al. 2019).

By definition, a prebiotic is "a substrate that is selectively utilized by host microorganisms conferring a health benefit." Compounds that affect the composition of microbiota through mechanisms that do not involve their selective use by host microorganisms for their growth, such as antibiotics, vitamins, and minerals, are not considered prebiotics. The health effects of prebiotics are evolving, but currently include benefits for the gastrointestinal tract, cardiometabolic, mental health, and bone (Gibson et al. 2017). Many fermentable carbohydrates have been reported to have prebiotic effects, but the most widely documented prebiotics to cause human health benefits are non-digestible oligosaccharides (Rastall and Gibson 2015).

Prebiotic compounds have been increasingly used by the food industry as functional ingredients in various preparations such as in the production of dairy products, confectionery, infant formulas, cereal bars, chocolate, and meat products, among others. To produce these compounds using hemicellulose from lignocellulosic biomass as a source of feedstock is a viable and sustainable alternative (Farias et al. 2019).

The focus of the chapter is to present the oligosaccharides chemical structure, physicochemical and biological properties, and production considering chemistry and enzymatic strategies. The applications of oligosaccharides were related to industrial production and future perspectives.

## 9.2 Chemical Structure and Composition

Oligosaccharides are a group of polymeric carbohydrates that can be found in free or combined forms. There are several types of oligosaccharides, differing from each other in their nature of monomeric sugars and named accordingly. Oligosaccharides are defined by IUB-IUPAC nomenclature as oligomers composed of 2 to 10 monosaccharides. Hemicellulose has a random combination of monosaccharides, the most common being D-glucose, D-mannose, D-xylose, and L-arabinose; therefore three main types of oligosaccharides can be derived from hemicellulose: xylooligosaccharides (XOS), mannan oligosaccharides (MOS), and arabinooligosaccharides (AOS) (Mussatto and Mancilha 2007; Belorkar and Gupta 2016).

XOS, oligosaccharides derived from xylan, are oligosaccharides composed of xylose chains linked by glycosidic β-1,4 bonds (Fig. 9.1). Their degree of polymerization can vary from 2 to 10, depending on the number of xylose residues, and are known as xylobiose, xylotriose, xylotetraose, xylopentaose, and so on. Besides xylose residues, xylan is commonly found in combination with other side groups

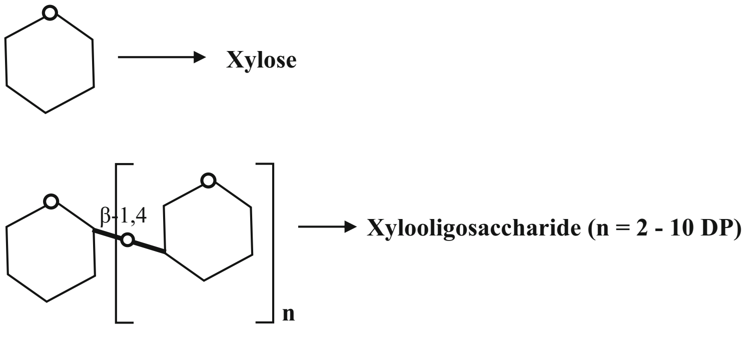

**Fig. 9.1** Xylooligosaccharide general structure

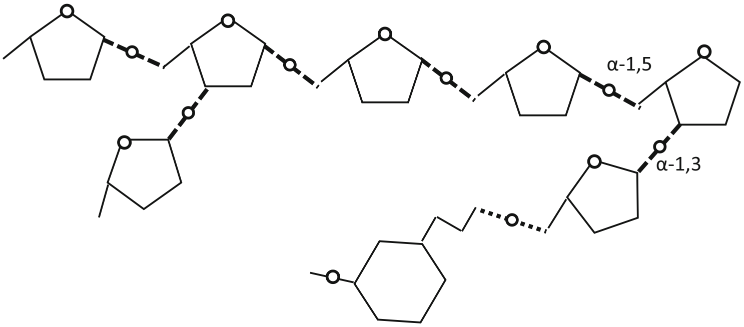

**Fig. 9.2** Arabinooligosaccharide structure

such as arabinofuranosyl, glucopyranosyl uronic acid, or acetyl groups, resulting in branched XOS with diverse properties and stability (Gupta 2012; Carvalho et al. 2013; Meyer et al. 2015; Ibrahim 2018).

Arabinooligosaccharides (AOS) are another class of oligosaccharides whose natural sources are arabinans present in plants cell wall components such as hemicellulose. They are branched pectic oligosaccharides comprised of α-1,5 linked backbone of L-arabinose residues, which can be substituted with α-1,2 and/or α-1,3 linked L-arabinose residues, the type of linkage depending on the source (Fig. 9.2). Also, from this group are the arabinoxylooligosaccharides (AXOS), isolated from xylan chains with a substitution of arabinose side chains (Westphal et al. 2010; Belorkar and Gupta 2016).

Mannan is a major constituent of hemicellulose from softwood. Mannan oligosaccharides can present a linear form, consisting of a C6 sugar, mannose, and backbone connected by β-1,4 glycosidic linkages, or it can present side chains of D-glucose or D-galactose linked to the main chain by α-1,6 bonds (Fig. 9.3), characterizing glucomannan oligosaccharides and galactomannan oligosaccharides, respectively (Singh et al. 2018; Bhatia et al. 2019).

## 9.3 Properties of Oligosaccharides

The physicochemical and physiological properties of each oligosaccharide can differ depending on the sugar residues present in the main chain, anomeric configuration, side groups, and linkage types. Usually, the polymer backbone of hexoses is more strongly bound than that of pentoses. Also, β-linkages are stronger than α-linkages that often generate the branches (Otieno and Ahring 2012b; Gullón et al. 2014).

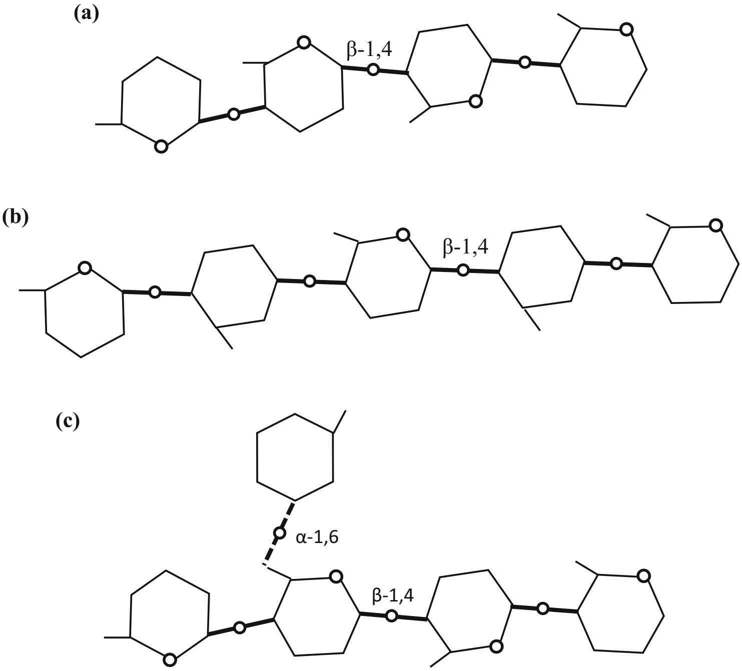

**Fig. 9.3** Mannan oligosaccharides structure. (**a**) Linear mannan oligosaccharide; (**b**) glucomannan oligosaccharide; (**c**) galactomannan oligosaccharide

### 9.3.1 Physicochemical Properties

Oligosaccharides are water-soluble and usually about 0.3 to 0.6 times as sweet as sucrose. Sweetness depends on the chemical structure and degree of polymerization; usually it decreases with longer oligosaccharide chains. The relative sweetness of XOS is 30% when compared to sucrose, while MOS and AOS can present 60% sucrose sweetness and none of them have an off-taste. This characteristic is highly exploited in food formulations as a sucrose substitute (Hirayama 2002; Samanta et al. 2015).

In some food production, the relatively low sweetness of oligosaccharides is desirable when a bulking agent is needed to enhance other food flavors. In the formulation of very sweet foods, for example, they can be used together with artificial sweeteners to mask the aftertastes produced by some of them. Besides, their higher molecular weight increases viscosity comparing with monosaccharides, which leads to an improved mouthfeel. Due to their high capacity to retain water, they can be used as humectants, since the reduction of water activity is convenient for microbial contamination control (Mussatto and Mancilha 2007).

Oligosaccharides are stable over a wide range of pH (2.0 to 8.0) and temperatures (up to 135 °C), which is a good feature for incorporations into foods; however higher pH and temperature than those can impair their physicochemical properties and

**Table 9.1** Physicochemical properties of oligosaccharides (xylooligosaccharides, mannan oligosaccharides, and arabinooligosaccharides) derived from hemicellulose

| Property | Xylooligosaccharides | Mannan oligosaccharides | Arabinooligosaccharides |
|---|---|---|---|
| Molecular formula | $C_{5n}H_{8n+2}O_{4n+1}$;<br>$n = 2$ to 10 | $C_{6n}H_{10n+2}O_{5n+1}$;<br>$n = 2$ to 10 | $C_{5n}H_{8n+2}O_{4n+1}$;<br>$n = 2$ to 10 |
| Molecular weight (g/mol) | 282 to 1338 | 342 to 1638 | 282 to 1338 |
| Relative sweetness | 30% of sucrose | 60% of sucrose | 60% of sucrose |
| pH stability | 2.5 to 8.0 | 2.0 to 7.0 | 2.0 to 7.0 |
| Temperature stability | Up to 135 °C | Up to 120 °C | Up to 135 °C |
| Melting temperature | 134 °C | 132 °C | 164 °C |
| Energy value (kcal/g) | 1.5 | 3.75 | 1.5 |

nutritional values. The stability in acid conditions, most likely to be found in the gastrointestinal tract, is also favorable for its use as prebiotics. Melting temperature was reported as 134 °C for XOS, 132 °C for MOS, and 164 °C for AOS (Gupta 2012; Samanta et al. 2015; Belorkar and Gupta 2016; Hu et al. 2016; Chacher et al. 2017; Gullon et al. 2017; Saville and Saville 2018) (Table 9.1).

Oligosaccharides can alter the freezing temperature of frozen foods. The antifreeze activity of xylobiose on the water at temperatures higher than −10 °C is greater than that of glucose, sucrose, and maltose. They are also able to control the intensity of Maillard reactions in heat-processed foods. The caloric value of oligosaccharides can usually vary from 1.5 to 2.0 kcal/g and are 40–50% lower than sucrose, which allows their use in anti-obesity diets, with the exception of mannan oligosaccharides which present a similar caloric value to sucrose. In addition, oligosaccharides present an acceptable odor and are non-cariogenic (Patel and Goyal 2011; Hu et al. 2016; Saville and Saville 2018).

## 9.3.2 Biological/Physiological Properties

XOS and MOS are known as non-digestible oligosaccharides (NDO), which means that they cannot be digested by humans since the human body lacks the enzymes required to hydrolyze the β-linkages present in these molecules. Because of this property, these oligosaccharides can be considered potential prebiotics, as they reach the gastrointestinal tract without being degraded and are available for the intestinal flora (Swennen et al. 2006; Bhatia et al. 2019).

For the metabolism of NDOs, bacteria present in the intestinal tract have to produce glycolytic enzymes to hydrolyze them into monosaccharides or disaccharides. These smaller molecules can be transported into the cell where they will be further metabolized to short-chain fatty acids (SCFAs), mainly acetate, propionate, and butyrate. Colon environment acidification is beneficial for the development of probiotic bacteria such as bifidobacteria and lactobacilli (Farias et al. 2019).

XOS, MOS, and AOS have similar effects to dietary fiber due to its indigestible quality and thus can prevent constipation. The SCFAs produced by the fermentation of these oligosaccharides by the colonic bacteria are efficiently absorbed and used by the human epithelial cells, stimulating their growth and water absorption, which consequently improves intestinal mobility. Besides, the high concentration of SCFAs lowers the colon pH enhancing the bioavailability of minerals, mainly calcium and magnesium. Besides, the increase in water absorption increases the solubility of some minerals (Mussatto and Mancilha 2007; Singh et al. 2015; Moreno et al. 2017).

Non-digestible oligosaccharides may also affect lipid regulation, since acetate and propionate influence cholesterol production, decreasing lipid and cholesterol blood levels. They also can influence glycemia by altering the absorption of macronutrients by delaying gastric emptying, thus preventing peak levels of blood glucose. Plasmatic glycemia is also affected by the bacterial production of SCFAs (Al-Sheraji et al. 2013).

NDOs can affect the mucosal immune system of the intestine, but their beneficial effects are not only confined to the intestinal tract. They can modulate both innate and adaptive immune mechanisms by incrementing the number of *Bifidobacteria*, which results in the production of anti-inflammatory metabolites and induces phagocytoses, protecting the organism against infections (Althubiani et al. 2018).

The use of NDOs in the animal feed industry, mainly for livestock, is increasing. Many factors can cause stress to the animals and compromise their normal microbiota, causing susceptibility to enteric diseases. The addition of antibiotics in feed often causes side effects and sometimes is even legally banned. However, some oligosaccharides, specialty MOS, can prevent the colonization of pathogenic bacteria more than stimulate beneficial microorganisms; therefore they can be a promising alternative for the use of antibiotics. In animals, NDOs are also able to enhance growth and feed conversion, as well as prevent early mortality (Swennen et al. 2006; Carvalho et al. 2013).

Several human and animal studies have been carried out to identify the potential health benefits of these oligosaccharides and to assess their possible intolerance and safety for consumption. For humans, studies have shown that the best daily intake for oligosaccharides is between 2 and 5 g. In animal models, the administration of a dose ranging between 7 and 10% of the diet did not show any adverse effects (Al-Sheraji et al. 2013; Samanta et al. 2015).

In summary, the consumption of NDOs such as XOS, MOS, and AOS, in the appropriate dosage, results in improvement of human and animal health, controlling the gut microbiota balance through the stimulation of beneficial bacteria growth, which also increases SCFA production. Thus, intestinal membrane integrity and minerals absorption are improved, as well as lower glycemic levels and improved immunity (Farias et al. 2019).

## 9.4 Production of Prebiotic Oligosaccharides

Xylooligosaccharides, mannan oligosaccharides, and arabinooligosaccharides are obtained by the hydrolysis of a natural polysaccharide, hemicellulose. However, due to the lignocellulosic biomass recalcitrance, a pretreatment for hemicellulose solubilization and its separation from the other structural components, cellulose and lignin, is required. To isolate hemicellulose, physical, thermal, or chemical methods can be used but despite the method, the final purpose is to obtain hemicellulose with desirable conditions for oligosaccharides production (de Freitas et al. 2019; Kruschitz and Nidetzky 2020).

### 9.4.1 Chemical Hydrolysis

Chemical pretreatments are widely used to obtain high sugar yields at low cost (Loow et al. 2016). It is possible to produce oligosaccharides of interest to the food, pharmaceutical, and chemical industries. This interest is due to their numerous health benefits, from lignocellulosic materials by methods such as acid hydrolysis, autohydrolysis, and alkaline extraction of polysaccharides followed by acidic or enzymatic hydrolysis (Fig. 9.4) (Brienzo et al. 2016). In chemical pretreatments in addition to the oligosaccharides of interest, unwanted and toxic substances such as monosaccharides and sugar degradation products can be produced, requiring a purification process (Ibrahim 2018; Khat-udomkiri et al. 2018; Wang et al. 2018b).

#### 9.4.1.1 Dilute Acid Hydrolysis

Dilute acid hydrolysis (Fig. 9.5) has the potential for large-scale oligomer production and is commonly used for biomass fractionation because it is efficient, cheaper, and faster than other methods. In addition, it can recover approximately 80% of sugars

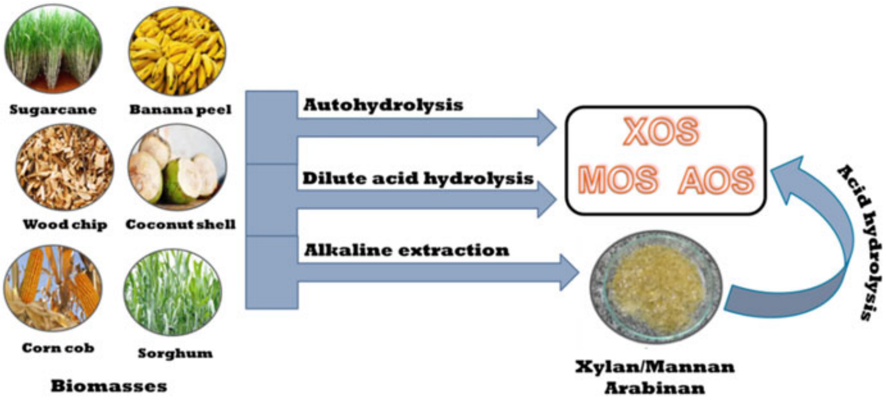

**Fig. 9.4** Chemical pretreatments of biomass for the production of xylooligosaccharides (XOS), mannan oligosaccharides (MOS), and arabinooligosaccharides (AOS)

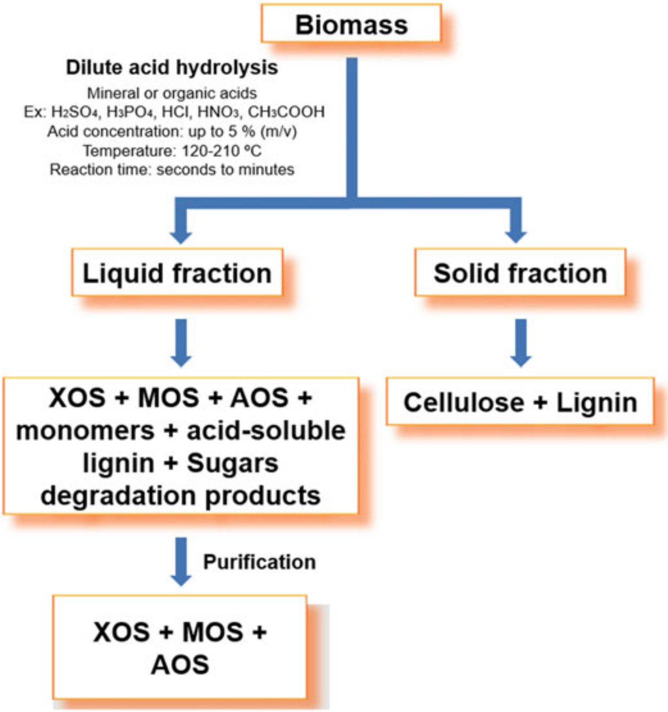

**Fig. 9.5** Schematic representation of lignocellulosic biomass acid hydrolysis for oligosaccharides production

from hemicellulose. Due to its glycosidic bonds and shorter chain, hemicellulose is the first hydrolyzed component of biomass. During hemicellulose breakdown, oligosaccharides are released and solubilized in the medium, whose composition can vary according to the biomass used. Sugarcane bagasse and corncob, which are xylan-rich raw materials, are often used for xylooligosaccharides (XOS) production; biomasses that have a greater amount of glucomannans or galactomannans, such as coffee grounds, release mannan oligosaccharides (MOS) and materials containing arabinan, such as rice straw, are hydrolyzed to obtain arabinooligosaccharides (AOS). The characteristics and degree of polymerization of the oligosaccharides formed during this process cannot be predicted, as they depend on the type of substrate used, conditions, and severity of the reaction (Yu 2007; Qing et al. 2013; Liu et al. 2019; Nopvichai et al. 2019).

In acid hydrolysis, monomers such as xylose, glucose, arabinose, mannose, and galactose are also released, as well as the acetyl and uronic groups of the hemicellulose chain (Willför et al. 2009). Cellulose undergoes few modifications under mild conditions due to its tight structure, high crystallinity, and degree of polymerization. After hydrolysis with dilute acid, cellulose is more accessible to cellulolytic enzymes, facilitating a further process of enzymatic hydrolysis (Shimizu et al.

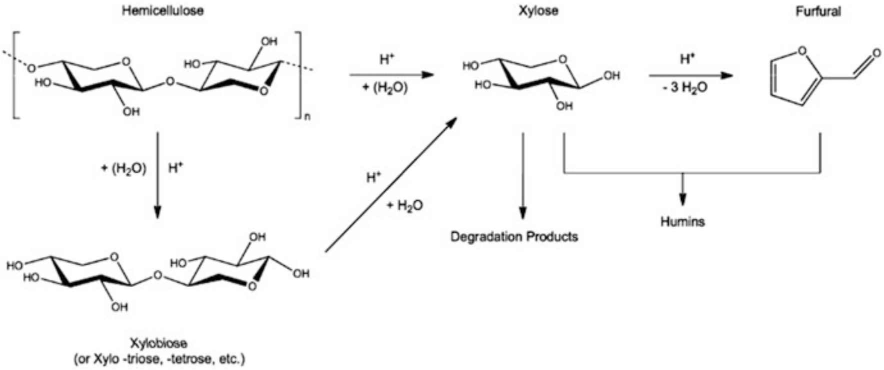

**Fig. 9.6** Production of xylooligosaccharides by xylan acid hydrolysis and formation of degradation products (Enslow and Bell 2012)

2020). Lignin, like cellulose, remains in the solid phase almost intact; only acid-soluble lignin, corresponding to approximately 5 to 10% of the total lignin, is solubilized (Mussatto 2016; Brienzo et al. 2017; Oriez et al. 2019; Schmatz et al. 2020; Świątek et al. 2020).

Indeed, a recent study by Marcondes et al. (2020) showed that hemicellulose-derived sugars yields are higher if the acid pretreatment is carried out in two stages. The first stage is performed with the objective of extracting the fast hemicellulose, while the second stage is performed to extract the slow hemicellulose. Thereby, the authors evaluated the acid hydrolysis of sugarcane bagasse at different conditions to maximize the solubilization and recovery of the hemicellulose in sugarcane bagasse as XOS with high selectivity. However, the results showed that the first stage yielded a XOS-rich, high purity hydrolysate and in the second stage only a xylose-rich hydrolysate could be obtained at high purity. The authors conclude that one strategy to reduce the high xylose production would be to identify the most suitable pretreatment for the target biomass with the aim to improve the XOS yield.

Diluted acid is preferred over concentrated acid for the production of XOS, MOS, and AOS because, although the rate of breakdown of the polysaccharide chain is lower and slower, there is a greater formation of oligosaccharides. Therefore, less amount of monosaccharides and undesirable products are formed. Moreover, diluted acids are generally less corrosive and toxic and, consequently, operating costs are lower. Another disadvantage of concentrated acid is the difficulty of recycling it after use and the risks involved (Otieno and Ahring 2012a; Baruah et al. 2018).

In more severe processes, along with degradation of hemicellulose or cellulose, the formation of by-products derived from the degradation can occur. Furfural, hydroxymethylfurfural, aldehydes, and phenolic acids are some of the by-products that can be produced and separated by osmotic filtration for use in industry. For example, furfural is used in the production of plastics, nylon, and lubricants. Levulinic acid can be used in solvents, polymers, pesticides, sedatives, and anxiolytics (Jiang et al. 2016; Zabot et al. 2019). Figure 9.6 shows the products formed during the acid-catalyzed hydrolysis of xylan.

In pretreatment with dilute acid, the acid usually at a concentration below 5% *(m/v)* is added to the biomass and the mixture is heated between 120 and 210 °C, with pressure up to 10 atm and time varying from seconds to minutes (Fig. 9.5). The sulfuric acid ($H_2SO_4$) is generally used in this type of pretreatment because it hydrolyzes biomass more efficiently. It is possible to recover high concentrations of hemicellulosic sugars with low concentrations of acid, reducing process costs (Loow et al. 2016).

Beyond sulfuric acid other mineral acids like hydrochloric (HCl), nitric ($HNO_3$), or phosphoric acid ($H_3PO_4$) are also studied. In comparison with sulfuric acid, it is possible to state that hydrochloric acid is more expensive and less efficient, more corrosive, and impacts the environment, factors that limit its use (Oriez et al. 2019). Nitric acid has the advantage of being less corrosive to stainless steel but is more expensive and some studies suggest that under optimized conditions there was less conversion of hemicellulose into sugars (Yang et al. 2015). Regarding phosphoric acid, there are not many studies about the fractionation of biomass, but its use for this purpose seems to be promising because of its ability to efficiently hydrolyze hemicellulose, besides being a safer and more beneficial alternative to the environment; however, it is the most expensive one (de Vasconcelos et al. 2013; Loow et al. 2016; Fontana et al. 2017; Oriez et al. 2019).

In addition to mineral acids, another alternative for the production of oligosaccharides is organic acids such as acetic, gluconic, oxalic, maleic, and citric, among others, which are advantageous due to higher oligosaccharides formation, lower xylose concentration, and degradation products such as furfural (Lin et al. 2017; Zhou and Xu 2019).

#### 9.4.1.2 Autohydrolysis

The main purpose of autohydrolysis (Fig. 9.7) is to solubilize hemicellulose, decrease the formation of unwanted products, and increase the accessibility of cellulose to cellulolytic enzymes. In autohydrolysis, also called liquid hot water (LHW) the biomass is hydrolyzed only using water under high temperature and pressure, between 150 and 230 °C and approximately 50 bar, respectively. Reaction time can vary between minutes and hours, and usually occurs in reactors; however recently microwave and steam explosion systems are being used for heating (Fig. 9.8) (Jeong and Lee 2015; Baruah et al. 2018; Kapoor et al. 2018; Wang et al. 2019).

The high temperature promotes the release of acetic and uronic acid in the medium due to the hydrolysis of acetyl and uronic groups present in the xylan and they act as catalysts increasing the xylan hydrolysis rate (Singh and Kalia 2017; Cano et al. 2020). The reaction (Fig. 9.9) is similar to what occurs in hydrolysis with dilute acid.

Hemicellulose is more susceptible to hydrolysis in this method due to its amorphous structure. In mild temperatures and short periods, hemicelluloses rich in xylan, mannan, and arabinan are hydrolyzed into high molecular weight

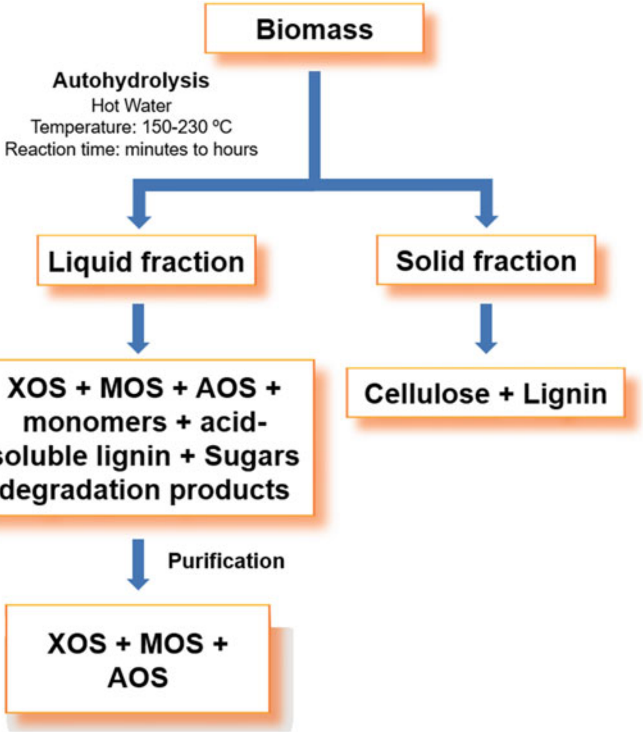

**Fig. 9.7** Schematic representation of lignocellulose biomass autohydrolysis for the production of oligosaccharides

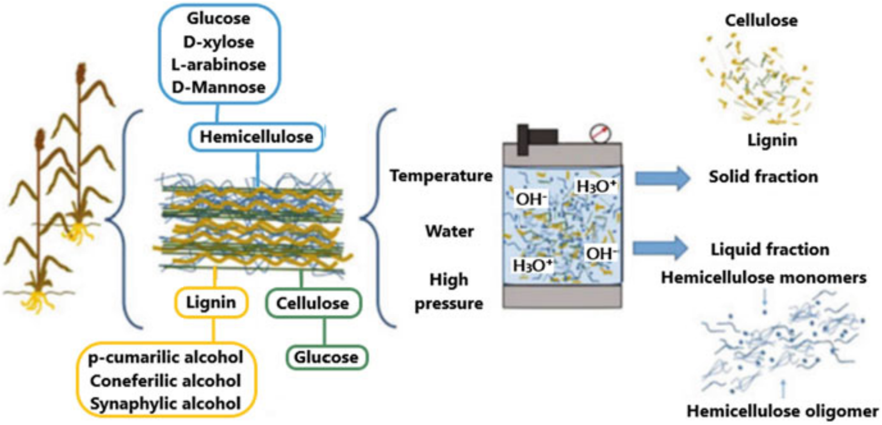

**Fig. 9.8** Autohydrolysis of lignocellulosic materials (Kapoor et al. 2018)

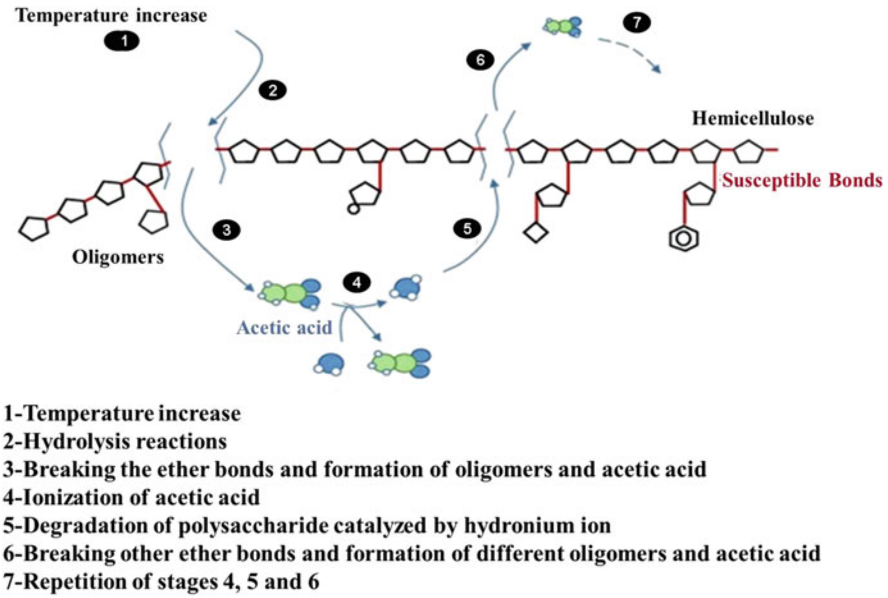

**Fig. 9.9** Hemicellulose chain breakdown in autohydrolysis. (Adapted from Amiri and Karimi 2018)

oligosaccharides that are soluble in the liquid fraction along with other hemicellulose sugars, such as xylose and arabinose. At higher temperatures, oligosaccharides are hydrolyzed to monosaccharides and sugar degradation products. In the temperature range usually used in autohydrolysis, there are few changes in cellulose and lignin structure. They remain in the solid phase, which can be recovered at the end of the process and hydrolyzed by enzymes. Above 230 °C the breakdown of cellulose chain into oligosaccharides and glucose is intensified and at 300 °C the conversion to glucose is almost complete (Ruiz et al. 2013; Gullón et al. 2014; Pielhop et al. 2015; Vallejos et al. 2015; Sarip et al. 2016; Kapoor et al. 2018). After the reaction, the hydrolysate is separated from the solid fraction and purified by removing the by-products to obtain high purity oligosaccharides (Chen 2015).

It is possible to obtain high yields of hemicellulose sugar oligomers, mainly from agricultural residues and herbaceous. Regarding woods, hardwoods are more susceptible to autohydrolysis than softwoods because they have more acetyl groups in the hemicellulose chain, delignification is more efficient, and there is less condensation of lignin. For the hydrothermal processes of softwoods, more severe conditions are necessary, due to the greater amount of lignin (Xiao et al. 2017).

This pretreatment is advantageous since it does not require the use of chemical, corrosive, and toxic reagents, preventing equipment corrosion and the need for chemical recycling. Only water is used, an environmentally friendly and low-cost solvent, reducing the need to use neutralizing chemicals. The costs of this pretreatment are lower compared to others. However, high temperature and pressure

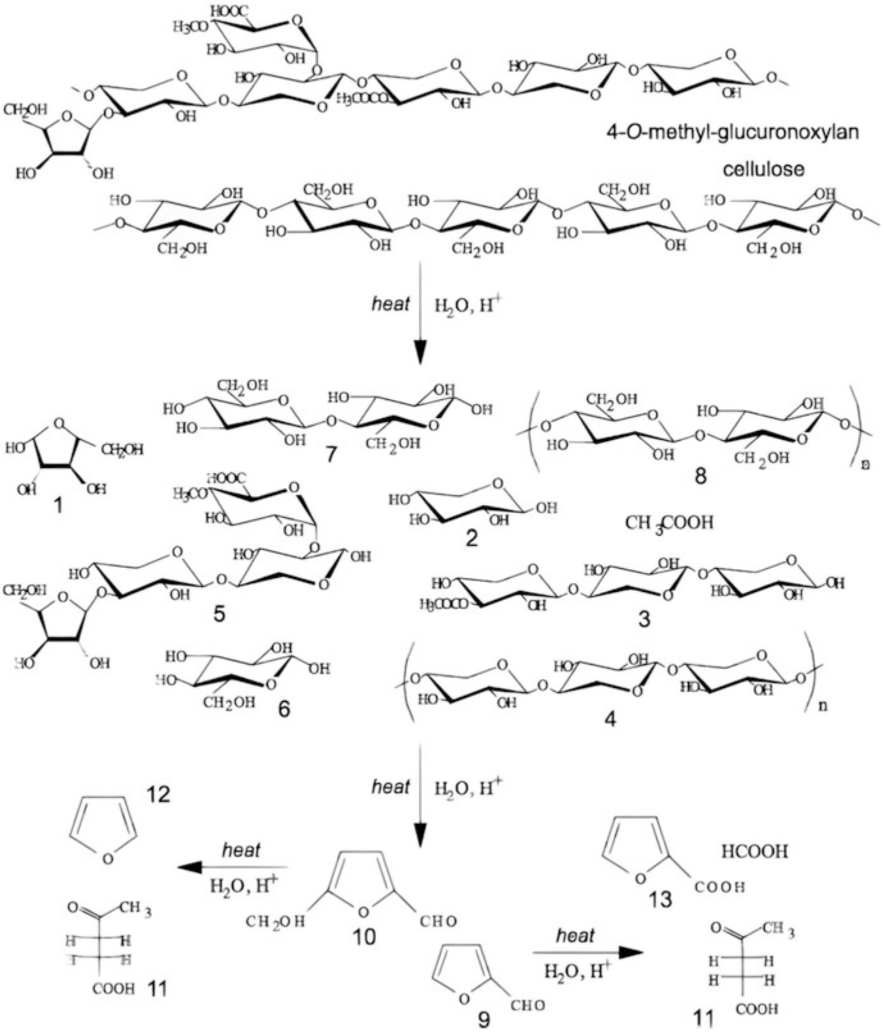

**Fig. 9.10** Products formed in the hydrothermal processes of 4-O-methylglucuronoxylan and cellulose: (1) arabinose; (2) xylose; (3) acetylated xylooligomers (DP of 3); (4) xylooligomers of higher molecular mass; (5) acidic, branched oligosaccharides; (6) glucose; (7) cellobiose; (8) cellooligomers; (9) furfural; (10) hydroxymethylfurfural; (11) levulinic acid; (12) furan; (13) 2-furoic acid (pyromucic acid); (14) formic acid; (15) acetic acid. (Adapted from Pereira Ramos 2003)

are conditions that are difficult to control and that can cause thermal degradation of hemicellulose (Fig. 9.10). This process, called pyrolysis, generates compounds that are not of interest such as furfural, derived from pentoses, uronic acids, and hydroxymethylfurfural (HMF) derived from hexoses, acetic, formic, levulinic acid, and lignin degradation products (Chen 2015; Pielhop et al. 2015; Vallejos et al. 2015; Tyagi et al. 2019; Wang et al. 2019).

#### 9.4.1.3 Alkaline Solubilization

Alkaline solubilization (Fig. 9.11) is a method to separate hemicellulose from the other lignocellulose components and use it for the production of oligosaccharides. First, the polysaccharide is solubilized with alkaline reagents and in the second step, it is hydrolyzed with dilute acid or enzymes (Brienzo et al. 2009; Loow et al. 2016; de Figueiredo et al. 2017).

This pretreatment is more effective for agricultural residues and herbaceous crops due to their lower amount of lignin, unlike woody biomasses. Alkaline reagents are used in the process such as sodium hydroxide (NaOH), ammonium ($NH_4(OH)$), magnesium ($Mg(OH)_2$), calcium ($Ca(OH)_2$), and potassium (KOH). A saponification reaction of ester bonds between lignin and hemicellulose occurs resulting in the removal and solubilization of lignin, removal of acetyl groups from hemicellulose, decrease in the degree of polymerization and crystallinity of cellulose, and swelling of its fibers, increasing its porosity and surface area, without its degradation. All of these factors facilitate access to carbohydrates by enzymes. Under certain conditions, hemicellulose is also removed from the biomass and solubilized allowing

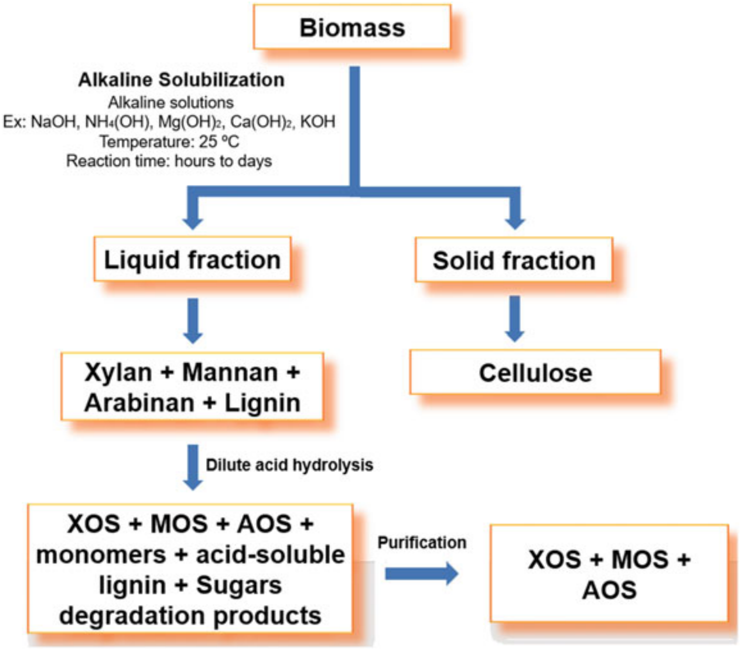

**Fig. 9.11** Schematic representation of lignocellulosic biomass alkaline extraction followed by acid hydrolysis for production of oligosaccharides

subsequent chemical or enzymatic processes to obtain XOS, MOS, and AOS (Harmsen et al. 2013; Devi et al. 2016; Baruah et al. 2018; Bochmann 2019).

NaOH is the most commonly used reagent due to its efficiency and when combined with oxidizing agents such as hydrogen peroxide ($H_2O_2$) and peracetic acid ($C_2H_4O_3$) the delignification process is increased, generating a solid fraction with greater enzymatic digestibility (Loow et al. 2016). The hydrogen peroxide in alkaline medium has been extensively studied for the production of bleached hemicellulose. In this method, the hydroxyl reacts with $H_2O_2$ forming hydroperoxyl anion ($HOO^-$) and superoxide ($O^-{}_{2)}$. The anion reacts with $H_2O_2$ that has not been dissociated to form hydroxyl radicals and superoxide oxidize and discolor lignin and break the ester bonds between hemicellulose and lignin, solubilizing them (Brienzo et al. 2016; Rabetafika et al. 2014).

The main advantage in alkaline methods is that the reactions occur under room temperature and pressure and process conditions are less severe compared to acid hydrolysis, causing less damage to equipment. In addition, polysaccharides are separated from other biomass components, increasing the efficiency of the enzyme during oligosaccharides production. The solid waste generated in the process is mainly composed of cellulose that can be used in the production of paper and cellulose derivatives or hydrolyzed into glucose by acids or enzymes and used in the production of biofuels. Another advantage is the possibility of recovering some bases such as calcium hydroxide that can be recovered as insoluble calcium carbonate after adding carbon dioxide in the aqueous medium. In this method, however, the sugar yield is low, there may be decomposition by alkali, the formation of undesirable products, reagent needs to be neutralized and recovered at the end of the reaction, and the process is slow, taking hours or days. High concentrations of alkali increase production costs and can be a concern for the environment (Devi et al. 2016; Loow et al. 2016; Khat-udomkiri et al. 2018; Chen et al. 2019).

### 9.4.2 Enzymatic Hydrolysis

In the last decades, enzymatic hydrolysis for oligosaccharide production and many other processes has been used as a substitute for chemical hydrolysis due to their work features, such as mild temperature (40–60 °C) and pH (4.5–6.0), high product yields (%), higher specificity, absence of corrosive effect, and for being environmentally friendly (Khat-udomkiri et al. 2018; Wang et al. 2018a; Amorim et al. 2019b; Satari et al. 2019).

Xylan and mannan are chemically complex and their depolymerization requires a set of enzymes called hemicellulases, among which there are specific enzymes for each glycosidic bond in the carbohydrate chain (Henrissat 1991). As well as for all hydrolase enzymes, hemicellulases catalyze the breakdown of glycosidic bonds using water as a proton transfer mediator to the free ends of the carbohydrates separated (Henrissat 1991; Nordberg Karlsson et al. 2018; Houfani et al. 2020).

Enzymes can be used in their free state in the reaction medium or immobilized in some adsorbent material. They can be immobilized on different supports as alginate beads, di-vinylbenzene copolymer, mesoporous silica, glyoxal agarose resin, polyethylene glycol hydrogel, among others (de Oliveira et al. 2018; Terrasan et al. 2018). The use of immobilized enzymes instead of free enzymes has the main advantage of allowing the reuse and recycling of them and can reduce the costs of the oligosaccharide production process. In addition, immobilization can increase enzyme stability, improves activity and selectivity, decreases inhibition by the product or other factors, and facilitates the purification process of oligosaccharides (de Oliveira et al. 2018; Sukri and Mimi Sakinah 2018; Terrasan et al. 2018).

Many microorganisms, mainly fungi and eubacteria, produce hemicellulases but they can be also produced by archaea and plants being founded, in this case, in seeds and fruits (Törrönen et al. 1992; Andrade et al. 2001; Kimura et al. 2002; Lisboa et al. 2006; Zhao et al. 2011; Terrone et al. 2018, 2020). Fungi are the most explored source of hemicellulases due to their ability to secrete metabolic products into the environment. For the industrial production of enzymes, mainly fungi and some species of bacteria are used (Jagtap et al. 2017; Satari et al. 2019). The main microbial producing hemicellulases used commercially are those of the genera *Trichoderma*, *Aspergillus*, *Bacillus*, and *Penicillium*. The enzyme systems of these microorganisms are reported to be inducible for the production of hemicellulases when specific components are present in the reaction medium (Törrönen et al. 1992; Soni and Kango 2013; Jagtap et al. 2017; Amorim et al. 2019b; Terrone et al. 2020). Microorganisms' hemicellulases producers, in general, are mesophilic but studies with extremophiles species have been carried out in search of enzymes with greater stability and properties such as very high or very low optimum pH and temperature (Andrade et al. 2001; Kumar and Satyanarayana 2015).

For industrial production of enzymes, in general, submerged fermentation methods are used because they allow better recovery of enzymes in the liquid medium, which are in an environment controlled in temperature and pH that preserves enzymes molecular properties (Jagtap et al. 2017; Álvarez et al. 2019; Satari et al. 2019). The enzyme production cost is still high compared to chemical products, which is still the bottleneck in the use of enzymes in most large-scale processes (Satari et al. 2019). In enzyme production, several factors must be considered and evaluated to obtain the highest amount of enzyme concentration possible released. The main factors that must be controlled are pH, temperature, substrate composition and concentration, agitation, and aeration (Battista and Bolzonella 2018; Khat-udomkiri et al. 2018; Terrone et al. 2020). Another factor that must be controlled during the production of hemicellulases is the product concentration, because in many natural microorganisms genetic systems the presence of monosaccharides or even some oligosaccharides represses the production of the enzyme of interest, reducing productivity (Battista and Bolzonella 2018; Satari et al. 2019).

Although the use of wild microorganisms has been carried out for many years in the field of enzyme production, still being a viable technology in some cases (Jagtap et al. 2017), the use of genetically modified microorganisms has expanded in research centers and enzyme production industries, through techniques such as that of recombinant DNA (Zhao et al. 2011; Soni and Kango 2013; Petrova and

Petrov 2017). The heterologous expression of hemicellulases through cloning provides a cheaper and simpler production, with a higher amount of enzyme recovered, and higher yield, besides facilitating the reaction conditions and their control, allowing more efficient recovery at the end of production (Zhao et al. 2011; Kumar and Satyanarayana 2015; Petrova and Petrov 2017).

Hemicellulases are a multi-enzyme system of depolymerizing and debranching enzymes that act synergistically in the hemicellulose hydrolysis and they are classified and named based on their substrate specificity and sometimes on their molecular mechanism (Nordberg Karlsson et al. 2018; Satari et al. 2019; Houfani et al. 2020). The specificity of enzymes for a single substrate occurs due to its complex three-dimensional conformation, which shapes to an active site responsible for catalyzing. In the active site, enzymes perform hydrolysis catalysis by two amino acid residues. One acts protonating the substrate, while the second performs a nucleophilic attack (inversion). The carboxylate group can also function as a general base, abstracting a proton from a nucleophilic water molecule which attacks the anomeric carbon originating a product with the retention of the configuration at the anomeric center (Battista and Bolzonella 2018; Nordberg Karlsson et al. 2018).

#### 9.4.2.1 β-Xylanases

These enzymes, also known as endo-1,4-β-D-xylanases or 1,4-β-D-xylan xylohydrolases (EC 3.2.1.8), cleave the glycosidic bonds in the xylan main chain releasing smaller non-substituted or branched xylooligosaccharides (2 to ~7 DP) and reducing xylan DP (Glibowski and Skrzypczak 2017; Wang et al. 2019). Microbial β-xylanases (fungal or bacterial) vary in molecular weight from 6 kDa to 150 kDa (Khanna and Gauri 1993; Bataillon et al. 2000; Kuramochi et al. 2016) and have pI values ranging from 1.7 to 9.5 (Krisana et al. 2005; Tanaka et al. 2005; Jalal et al. 2009). Most β-xylanases have optimum acidic pH (Decelle et al. 2004; Knob and Carmona 2010; Jnawali et al. 2018), but exceptions can be found (Mamo et al. 2009; Hwang et al. 2010). Almost all described have only one subunit and, in most cases, are glycosylated (glycoproteins) (Nordberg Karlsson et al. 2018; Terrone et al. 2020).

β-xylanases are extremely dependent on the presence of accessory enzymes in the reaction medium, and they can differ from each other in relation to their specificity by bonds in the xylan backbone (Bajpai 2014; Braga et al. 2014; Terrone et al. 2020). Some of these enzymes cut glycosidic bonds of the main chain randomly at unsubstituted regions of the substrate, but most of them select bonds for hydrolysis depending on the nature of the substrate, chain length, branched substituents, etc. (Bajpai 2014; Brienzo et al. 2016; Khat-udomkiri et al. 2018; Sukri and Mimi Sakinah 2018). Their connection to the substrate also depends on the substituents on the xylose residues neighboring the attacked residues to guide themselves to the substrate binding, having little or no action against linear xylose backbone unsubstituted (Bajpai 2014; Nordberg Karlsson et al. 2018).

β-xylanase can be classified as specific or cross-specific. With specificity for the substrate, its action is restricted to β-1,4 bonds in xylans, and when it has cross specificity it can also catalyze the hydrolysis of β-1,4 bonds in other polymers such

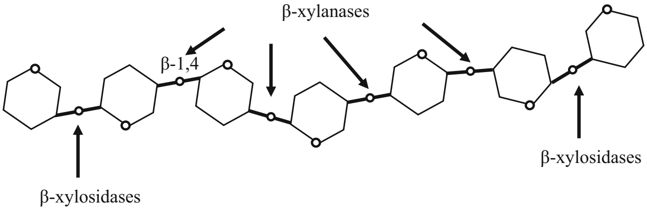

**Fig. 9.12** β-xylanases and β-xylosidases active sites in debranched xylan

as carboxymethyl cellulose (Bajpai 2014; Nordberg Karlsson et al. 2018). Therefore, β-xylanases catalyze the hydrolysis of xylans and xylooligosaccharides (Fig. 9.12), and its action results in β-D-xylopyranosyl oligomers with a DP of more than 4 xylose residues with substitution groups or not, depending on the substrate, but also they can release xylose, xylobiose, and xylotriose (Sukri and Mimi Sakinah 2018; Wang et al. 2018a; de Freitas et al. 2019; Houfani et al. 2020). The efficiency with which they hydrolyze oligosaccharides decreases with decreasing DP or with increasing substrate concentration (Khat-udomkiri et al. 2018; Wang et al. 2018a). Most β-xylanase works via a retaining mechanism with a double displacement (Braga et al. 2014; Nordberg Karlsson et al. 2018).

Endo-1,4-β-xylanases are different in their structure, mode of action, physicochemical properties, and substrate specificities. They are currently classified under GH families 5, 7, 8, 10, 11, 30, 43, 51, and 98. Xylanases from family 10 generate more xylose than xylanases from family 11. Xylobiose and substituted xylotriose are the main products of family 10, while xylobiose, xylotriose, and substituted xylotetraose are the main products of family 11. The GH30 family contains xylanase specialized in the cleavage of linear parts of xylan and requiring a MeGlcA substitution on the xylan chain as well, whereas xylanases found in the GH5 family does not attack linear xylan and depends on substitution in position 3 of xylose, but very little is known about the mode of action of this enzyme (Biely et al. 2016; Katsimpouras et al. 2019).

β-xylosidases are enzymes very specific for xylooligosaccharides generated by the action of β-xylanase and other hydrolases that are not substituted and have a DP up to 4. This enzyme acts from the non-reducing end, releasing D-xylose as the single product of its hydrolysis (Fig. 9.12). Thus, for xylooligosaccharides production this enzyme is not desired due to the degradation of the oligosaccharides, decreasing the yield of XOS, and the inhibition effects that they may cause in XOS production (Petrova and Petrov 2017).

### 9.4.2.2 β-D-Mannanases

Mannans are linear or branched-chain polysaccharides, which can have a single type of sugar in their main chain or several types, a heteropolymer (Singh et al. 2018; Bhatia et al. 2019). Mannan backbone degradation depends on the action of the depolymerizing β-mannanase that hydrolyzes β-1,4-linked mannose residues of galacto(gluco)mannans, releasing mannan oligosaccharides (Fig. 9.13) (Soni and

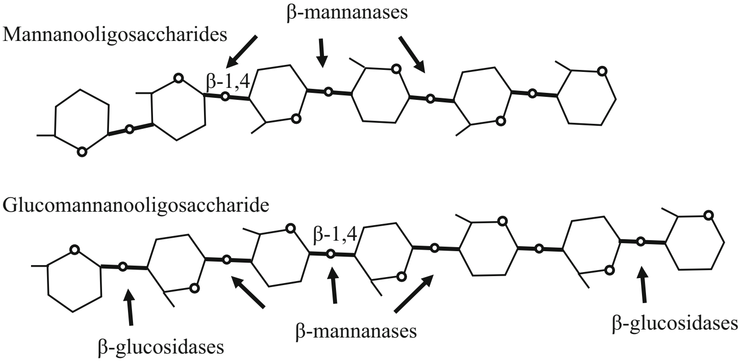

**Fig. 9.13** β-mannanases active sites in debranched mannan ooligosaccharides and β-mannanases and β-glucosidases active sites in debranched glucomannan oligosaccharides

Kango 2013; Nopvichai et al. 2019). The activity of these enzymes, also known as mannan endo-1,4-β-mannosidase or 4-β-D-mannan mannanohydrolase (EC 3.2.1.78), varies with the number and distribution of substituents in the carbohydrate chain, and with the glucose/mannose ratio. β-D-mannanases can vary in size from 18 kDa to 162 kDa. They have a wide range of pI and optimal pH (from acid to basic) (Cho et al. 2006; Lisboa et al. 2006; Chen et al. 2007; Blibech et al. 2010; Zhou et al. 2018).

As well as xylans, for the complete degradation of mannans, accessory enzymes are needed to act on the branches of the chain. These enzymes are β-mannosidase, β-glucosidase, α-galactosidase, and acetyl esterase. β-mannanase is the most active enzyme on mannans with few substitutions of galactose residues. This galactose residue blocks the access of β-mannanase to the mannose backbone especially if these residues are on alternate sides in the main chain. Once galactose substitutions are on the same side of the chain, the hindering effect of β-mannanase access to the main chain is reduced. The products of β-mannanase hydrolysis are mainly oligomannan or oligoglucomannan (4–5 DP) but also mannobiose and mannotriose can be released. The presence of galactose substitutions in the mannose residues adjacent to the ends hinders the action of these enzymes, reducing their activity (Soni and Kango 2013; Rahmani et al. 2017; Nopvichai et al. 2019; Houfani et al. 2020).

In addition to the ability to hydrolyze glycosides, β-mannosidases also have transglycosylation activity, which is, in this case, the synthesis of mannan oligosaccharides and another specific oligosaccharide through the binding of β-glycosides (Schröder et al. 2006).

#### 9.4.2.3 Debranching Enzymes (Accessory Enzymes)

Contrasting enzymes that act on the polysaccharide main chain, the substituents are liberated by accessory enzymes, glycosidases, and esterases that hydrolyze the bonds between the main chain and its substituents or the side chains of these backbones. According to hydrolysis characteristics, the accessory enzymes can be divided into enzymes that attack the substituents whether they are present in polymers or oligomers; and enzymes that do not act on polymeric substrates, being active only in branched or substituted oligosaccharides, generally generated by the action of β-xylanase or β-mannanase.

#### 9.4.2.3.1 α-Arabinofuranosidase

Enzymes that remove non-reducing α-L-arabinosyl residues of arabinans, arabinoxylans and arabinogalactans, with great specificity for the substrate, and can release arabinose from the various substrate (Fig. 9.14). α-Arabinofuranosidases can be monomeric, dimeric (2 subunits), tetrameric (4 subunits), and octameric (8 subunits) with molecular weights reaching from 49 to 530 kDa, isoelectric points from 3.5 to 9.7, and optimal pH values range from 2.3 to 7.4 (Hespell and O'Bryan 1992; Margolles and De Los Reyes-Gavilán 2003; Inácio et al. 2008; Terrone et al. 2020). Some characteristics of the substrate that influence α-arabinofuranosidase activity are the substitutions of arabinose in the main chain and the DP. Most of these enzymes release only arabinose residues linked by α-1,3 bonds to the main chain. Others can act on bonds α-1,2, α-1,3, and α-1,5 (exo α-L-arabinofuranosidase EC 3.2.1.55). Some α-arabinofuranosidases release arabinose residues linked by α-1,2 or α-1,3 bonds specifically from xylose residues with a single substitution (Houfani et al. 2020).

Some of these enzymes release arabinose only from terminal xyloses or from xylooligosaccharides (4–5 DP), while others are able to release arabinose from nonterminal, from the intact polysaccharide (endo α-L-arabinofuranosidase EC 3.2.1.99). These characteristics mean that α-arabinofuranosidase can be divided into those involved in the degradation of arabinoxylans and those that are "arabinose-releasing" enzymes, which act on different substrates regardless of their composition. In a study by Terrone et al. (2020), the action of an α-arabinofuranosidase produced by *Aspergillus hortai* on oat xylan (arabinoxylan) for the production of oligosaccharides was reported, and the release of arabinoses in the reaction medium was observed, mainly when purified α-arabinofuranosidase was associated with an endoxylanase. α-arabinofuranosidase that releases arabinose residues from

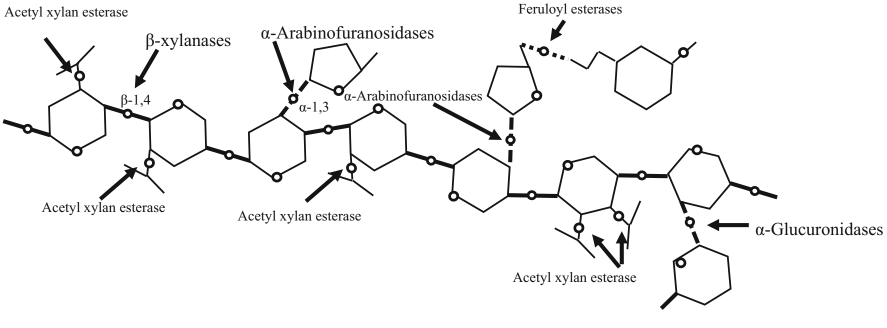

**Fig. 9.14** Xylan-degrading enzymes active sites in branched xylan

arabinoxylans in the absence of β-xylanases was reported by Kormelink et al. (1991) but they are rare.

#### 9.4.2.3.2 α-Glucuronidase

These enzymes remove D-glucuronosyl residues or 4-O-methyl-D-glucuronosyl residues with α-1,2-glycosidic bond, from the xylan backbone (Fig. 9.14). There are very few α-glucuronidases (EC 3.2.1.131) described in the literature in relation to β-xylanases for example. Despite this, the α-glucuronidases described have a diversified optimal pH rate, varying between 4 and 8 but most of them prefer acidic media (Xue et al. 2008; Rosa et al. 2013; Rogowski et al. 2014; Septiningrum et al. 2015). α-Glucuronidases have activity mainly in glucuronoxylans and arabinoglucuronoxylans and most of those described have a preference for smaller oligosaccharides (2–6 DP) with little activity in polysaccharides and oligosaccharides with a DP greater than 10 (Lee et al. 2012; Rogowski et al. 2014; Houfani et al. 2020), but some exceptions have been described (Yan et al. 2017). The activity of these enzymes is highly inhibited by the presence of other adjacent substituents in the oligomer, especially acetyl groups (Chong et al. 2015).

#### 9.4.2.3.3 Galactosidase

Galactosidase is a group of enzymes that hydrolyze the D-galactoses binding of oligosaccharides. They are classified into α-galactosidase (EC 3.2.1.22) that acts on α-1,6 glycosidic bonds of galactose branching linked to galacto(gluco)mannan main chain (Fig. 9.15), releasing D-galactopyranosyl residues (Jindou et al. 2002; Soni and Kango 2013; Houfani et al. 2020), and β-galactosidase (EC 3.2.1.23) that catalyzes the hydrolysis of β-galactosyl from the non-reducing end of several oligosaccharides especially pectin galactans, or synthesized oligosaccharides by transgalactosylation of lactose dimers (Cho et al. 2003; Kaneko and Kobayashi 2003; Petrova and Petrov 2017). The use of α-galactosidase is more relevant in the mannan oligosaccharide production process due to its action on hemicellulose. α-Galactosidases have a wide

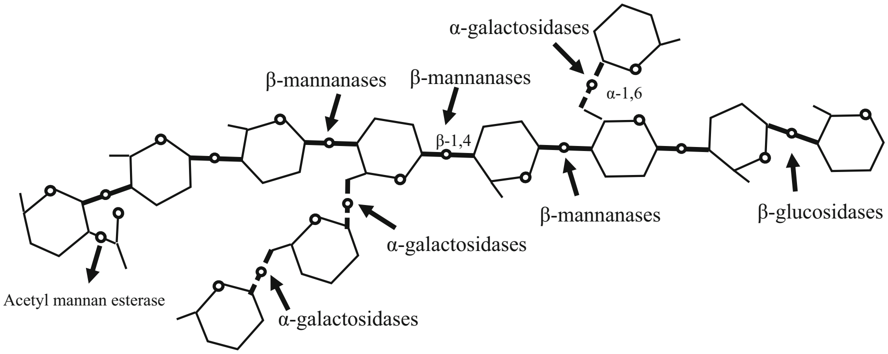

**Fig. 9.15** β-mannanases, β-glucosidases, and α-galactosidases active sites in branched galactoglucomannan

range of optimal pH and isoelectric points, varying between 3 and 8 (Shibuya et al. 1997; King et al. 2002; Wang et al. 2010).

The presence of α-galactosidase in the reaction medium is important for the production of mannan oligosaccharides because this enzyme acts on the main chain releasing galactose residues and preparing the substrate for mannanases. Some enzymes in this group release galactose from long polymer chains of larger galactomannans and oligosaccharides while others show greater affinity for small branched oligosaccharides (Wang et al. 2010).

#### 9.4.2.4 Synergy and Enzymatic Cocktails for the Production of Xylan/ Mannan Oligosaccharides

The production of oligosaccharides via enzymatic hydrolysis, from branched polymeric substrates, such as xylans and mannans, depends on a complex of cooperative or synergistic enzymes. This complex presents a variety of chain and side chain-cleaving enzymes of different specificities that are responsible for cleaving the different bonds present in those substrates (Houfani et al. 2020). For both depolymerizations of xylans and mannans, the set of enzymes consists of the main enzyme, which will attack the bonds of the polysaccharide backbone, and two or three debranching enzymes that create new sites on the main chain, thus helping major enzymes in accessing their substrate. At the same time, the action of the main-chain cleavage enzyme facilitates the activity of accessory enzymes, since they reduce solution viscosity and increase the diffusion of the substrate in the medium by decreasing the degree of polymerization (Álvarez et al. 2019). The synergy phenomenon can be observed either when purified main-chain or debranching enzymes are used (Jagtap et al. 2017).

The synergy between two or more enzymes occurs when the presence of one enzyme in the reaction medium enables or enhances the action of the other enzymes (Van Dyk and Pletschke 2012; Terrone et al. 2020). As reported by Soni and Kango (2013), the synergy between two or more enzymes can be classified into homosynergy and heterosynergy. Homosynergy is observed when the mixture of two (or more) enzymes that catalyze main-chain bonds, or two (or more) debranching enzymes with different specificities, results in a greater quantity of products than the sum of products released by the enzymes applied separately (Kumar and Wyman 2009; Van Dyk and Pletschke 2012). This effect can occur between two main-chain cleavage enzymes, for example, a β-mannanase and a β-mannosidase, or between two or more debranching enzymes (Soni and Kango 2013; Amorim et al. 2019a). In some cases, a substituent can hinder the action of removing another substituent in the neighborhood by accessory enzymes. In this type of synergistic interaction, it is considered that the action of one enzyme provides the substrate for the other enzyme or allows the other enzyme access to its substrate (Battista and Bolzonella 2018).

However, some main-chain cleavage enzymes may require the prior action of an accessory enzyme. This is called heterosynergy. An example of this is when an enzyme that attacks the polysaccharide backbone is unable to access its substrate in the presence of substituted glycoside residues. The presence of these substituents decreases the catalytic efficiency of the enzyme by blocking access. In this case, the accessory enzymes act by releasing the substituents from the main chain, allowing an increase in enzyme activity that reduces the degree of polymerization (Terrone et al. 2020). Therefore, heterosynergy is when the mixture of one (or more) degrading enzyme from the main chain and one (or more) debranching enzyme is more efficient in releasing hydrolysis products than when these enzymes are used individually (Soni and Kango 2013).

Synergistic studies between enzymes and also studies on the sequence with which the enzymes work more efficiently have increased in recent years to obtain greater production of xylooligosaccharides (Wang et al. 2010; Álvarez et al. 2019; Terrone et al. 2020). In these studies, it is possible to evaluate the physical barriers that the enzymes encounter to access their substrate and also the characteristics of the substrate recalcitrance. In addition to the synergy of the enzymes, the proportions of each enzyme and the sequence that each enzyme will be applied in the reaction medium are also relevant. The results may differ when the enzymes are used in sequence, and not simultaneously. That is why sequential studies about the performance of each enzyme are important for the synergistic effect between them to generate an amount of product as largest as possible. This strategy reduces the cost of reaction by reducing the required enzyme load, which is often wasted and allows obtaining more efficient enzymatic cocktails for the hydrolysis of polysaccharides (Satari et al. 2019).

For the production of xylooligosaccharides, the synergistic action usually occurs between endoxylanases, α-arabinofuranosidase, and glucuronidases for the majority of glucuronoarabinoxylans, especially if these substrates were treated with some type of pretreatment that removes other substituents such as ferulic acids and acetyl groups (Braga et al. 2014; Khat-udomkiri et al. 2018; Álvarez et al. 2019; Terrone et al. 2020). Generally, the pretreatments used for the production of XOS, which precede enzymatic hydrolysis, are the alkaline extractions in the presence of potassium hydroxide (KOH), sodium hydroxide (NaOH), calcium hydroxide ($Ca(OH)_2$), or ammonia, because they separate hemicelluloses from other lignocellulosic material components, preserving their characteristics and making them more available for the action of hemicellulases (Petrova and Petrov 2017; Chen et al. 2018; Jnawali et al. 2018; Khat-udomkiri et al. 2018; Satari et al. 2019). Using β-xylanases alone in the reaction medium release several types of heterogeneous xylan fragments, containing xylose oligomers in their composition substituted with arabinose, uronic acids, or acetylations (Bajpai 2014; Amorim et al. 2019a). Associated with debranching enzymes, the variety of fragments decreases and xylanases are able to release more homogeneous xylose oligomers.

Regarding the production of mannan oligosaccharides from galactomannans or galactoglucomannans, the presence of at least one debranching enzyme, like α-galactosidases or acetylmannanesterases, is required to act together with β-mannanases, which are strongly blocked by the presence of galactose substitutions and acetyl groups in the main chain (Wang et al. 2010; Soni and Kango 2013).

Due to the synergistic use of different enzymes in the reaction medium, it is crucial to combine the catalytic and physical-chemical properties of each enzyme before their use in the industrial oligosaccharide production processes. Properties such as temperature, reaction time, sequence of addition of each enzyme, and especially optimal pH of activity must be combined and controlled for efficient obtaining of xylan/mannan oligosaccharides.

### 9.4.3 Industrial Production

The market for oligosaccharides has grown in recent years, mainly in countries such as China and Japan but also in Europe; however, few companies produce these compounds industrially nowadays. Xylooligosaccharides are the oligosaccharides from hemicellulose most produced worldwide, with China as the main consumer country. Since 2003, the use of XOS as a feed additive in the livestock industry is approved by the Ministry of Agriculture of the People's Republic of China, which has caused the increased consumption of the oligosaccharide in the country. In 2015 the consumption of XOS as additives in animal feed in China was 1600 tons (CCM Data and Business Intelligence 2016).

Longlive Bio-Technology Company Ltd., located in China, occupies a leading position worldwide with regard to the production capacity of xylooligosaccharides. They are able to produce 4000 tons per year and another production line is being constructed with a capacity of 6000 tons per year. The raw material used for the production of XOS is the corn cob; however, the company also uses it in the manufacture of several other products such as dextrose, maltose, maltodextrin, sorbitol, xylitol, xanthan gum, etc. (China Food Additives and Ingredients Association 2010).

Henan Heagreen Bio-technology Co., Ltd., founded in 2014, is another functional oligosaccharide producer in China. The main business of Heagreen is xylooligosaccharides production and sales as well as related services. It is the only company specializing in the production, research, and development of XOS in the world. Enzymatic hydrolysis, using a multi-enzymatic complex, is the technology used by this company to transform the raw material (corn cobs) into oligosaccharides. For the purification and concentration of the molecules, a membrane integration technology is used, a low-energy, environmentally friendly method. Finally, the product is dried through a vacuum low-temperature drying technology, which makes the product have the characteristics of high density and strong anti-hygroscopic performance (Henan Heagreen Bio-technology 2015).

Pilot-scale production of xylooligosaccharides from *Miscanthus* was conducted using steam explosion pretreatment and enzymatic hydrolysis. To evaluate XOS generation, parameters such as temperature and reaction time were varied, considering the effects on sugar recovery and formation of fermentation inhibitors. XOS yields up to 52% (w/w of initial xylan) were obtained under the steam explosion conditions studied (200 °C; 15 bar; 10 min). A commercial endoxylanase was responsible for the production of xylobiose from XOS-rich hydrolysate (380–500 g/kg of initial xylan), which is the XOS with the highest prebiotic potential. Under the conditions which yielded the highest amount of XOS, the production of degradation compounds such as HMF and furfural was low, 0.2 g/L and 0.3 g/L respectively. Another pilot-plant production of xylooligosaccharides from corncob was carried out by steaming and enzymatic hydrolysis. It was able to obtain 74.5% of XOS in the final product, mainly comprised of xylobiose and xylotriose. This information shows that this method was successful in producing xylooligosaccharides with prebiotic action and has the potential to be applied on an industrial scale (Yuan et al. 2004; Bhatia et al. 2020).

Considering the situation in Brazil, where 140,000 tons of sugarcane bagasse are produced from ethanol production, this would be a raw material with high potential for the production of xylooligosaccharides. If a hydrothermal treatment were used to solubilize sugarcane bagasse xylan in the form of XOS, with a yield of 43.6%, it would be possible to produce 14,000 tons of XOS per year (Carvalho et al. 2018).

The increased yields of XOS may lead to new uses for the xylan derivatives, besides the benefits of human/animal health. For example, adsorption studies of XOS on kraft pulp fibers revealed positive effects on pulp yield (Cornetti et al. 2020), beating, and pulp strength properties (Ban et al. 2011). These results support the theory that XOS enters most pores in the fiber to a greater extent than high-molecular-weight xylan does. To some extent, these properties can help to meet various needs in the large pulp and paper market.

## 9.5 Conclusions and Future Perspectives

The development of biorefineries is becoming progressive in the last years because of the ideal to use renewable resources to obtain food, chemicals, and fuels. Therefore, biomass has been considered a resource of utmost importance. Polysaccharide-related residues are a great source for bioactive compounds, oligosaccharides being one of them. Oligosaccharides derived from hemicellulose are recognized as competitive emerging prebiotics and the use of lignocellulosic biomass as raw material for their production is considered a potential strategy to reduce production costs.

The global prebiotics market reached US$ 2.90 billion in 2015 and US$ 4.24 billion in 2017. This market is expected to grow approximately 12.7% by 2025 profiting around US$ 10.55 billion (Mano et al. 2018; Bhatia et al. 2020; Hurtado-Romero et al. 2020). From 1997 to 2008, about 32 products containing oligosaccharides from hemicellulose, mostly XOS, were launched. However, XOS market price (1–200 US$/kg) is yet higher when compared to other oligosaccharides such as fructooligosaccharides (1–20 US$/kg), galactooligosaccharides (5–100 US $/kg), and inulin (10–100 US$/kg). Therefore, several types of research are being developed in order to produce a pure form and high yield of these oligosaccharides from different types of hemicellulose-containing substrates in a cost-effective way. These novel production strategies can be further integrated into biorefinery processes.

**Acknowledgments** The authors thank the São Paulo Research Foundation (FAPESP grant number 2017/22401-8; 2019/12997-6) and CNPq (303416/2018–1) for research support.

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# 10

# Advances and New Perspectives in Prebiotic, Probiotic and Symbiotic Products for Food Nutrition and Feed

Franciane Cristina de Figueiredo and Pedro de Oliva-Neto

## Abstract

The gastrointestinal tract is colonized by several bacteria that are directly associated with the well-being of the host. Bacteria related to the balance of intestinal flora are often used as dietary supplements, known as probiotics. Other products marketed as a functional ingredients are the prebiotics, nondigestible oligosaccharides known to selectively stimulate the growth of beneficial bacteria. Prebiotics such as xylooligosaccharides (XOs), fructooligosaccharides (FOs), and galactooligosaccharides (GOs) can be found naturally in fruits, vegetables, honey, and milk or industrially produced, such as XOs, obtained by the extraction and hydrolysis of hemicellulose derived from lignocellulosic materials. There are also symbiotic products, which consist of added probiotic strains in prebiotic foods or ingredients. These types of ingredients can maintain homeostasis in the intestinal microbiota preventing the onset of some diseases, in addition to being considered an alternative to the use of antibiotics to treat some infections. Comprehending the action mechanisms of these ingredients is important for understanding various diseases and for formulating products that are effective in maintaining equilibrium of microbiota. The present review seeks to bring the most up-to-date research and advances in food nutrition involving intestinal microbiota as well as prebiotics, probiotics, and symbiotics.

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**Keywords**

Intestinal microbiota · *Lactobacillus* · *Bifidobacterium* · Xylooligosaccharides · Fructooligosaccharide · Galactooligosaccharides

## 10.1 Introduction

The intestinal microbiota is largely related to health and the manifestation of diseases in animals. Important advances in the health field have shown that the microbiota is linked to important metabolic activities, and changes in its composition can lead to serious diseases (Wang et al. 2017; Quigley 2019). Currently, researchers seek to discover and develop new products that help or modulate the proper functions of the organism. Therefore, the target of many researches is to try to maintain the homeostasis of the intestinal microbiota. Among the ingredients that develop such functions are prebiotics, probiotics, and symbiotics (Sanders et al. 2019a).

These types of ingredients are considered an alternative to the use of antibiotics in the treatment of some diseases, for example, salmonellosis, which are infections caused mainly by *Salmonella enterica* serovar *Typhimurium* (*Salmonella typhimurium*) and *Clostridium difficile*, with more than one million cases reported annually (Sanders et al. 2019a, b).

Recent discoveries show that maintaining the homeostasis of the microbiota is fundamental to the host's well-being, but little is known about how these microorganisms act to generate such benefits, nor how the composition of the intestinal flora influences certain diseases. Furthermore, many of the modulators of intestinal flora (prebiotics, probiotics, and symbiotics) do not have all their mechanisms of action well understood. These types of ingredients still need to be deeply studied to elucidate relevant issues such as the specificities of action in different genera of microorganisms and the doses stipulated for their proper functioning.

The purpose of this review is to present the most up-to-date concepts of prebiotics, probiotics, and symbiotics, as well as updating the understanding of the mechanisms of action related to them and situating the latest advances in research that assess the microbiota-health-disease interaction.

## 10.2 Prebiotics

### 10.2.1 Definition and Classification

Gibson and Roberfroid (1995) used the term "prebiotic" to define nondigestible oligosaccharides capable of stimulating the beneficial bacteria growth (probiotics). Although this concept has been revised a few times, the main idea has been maintained over the years (Rastall and Gibson 2015; Hutkins et al. 2016). Recently in 2016, the term was updated in a consensus of experts gathered by the International

Scientific Association for Probiotics and Prebiotics (ISAPP). The new definition presents prebiotics as “substrate that is selectively used by host microorganisms conferring health benefit” (Gibson et al. 2017). Generally these oligosaccharides have short chains of 2 to 12 simple linked sugars and are sweet and soluble in water depending on the degree of polymerization and molecular mass; however substances such as polyphenols and polyunsaturated fatty acids can also have a prebiotic effect (Manning and Gibson 2004; Markowiak and Śliżewska 2018; Sanders et al. 2019b).

The presence of β-type bonds is what makes these oligosaccharides nondigestible, since most living beings do not have enzymes capable of degrading this type of bond (Carvalho et al. 2013). Because prebiotics reach the intestine intact, they serve as a substrate for nonpathogenic bacteria, usually of the genus *Bifidobacterium* and *Lactobacillus*, promoting a change in the composition of the intestinal flora (Markowiak and Śliżewska 2018).

These oligosaccharides can become an alternative to the use of probiotics, because their handling is less laborious, besides being more economically accessible, such as fructooligosaccharides and galactooligosaccharides (Macfarlane et al. 2006).

Interest in the commercialization of prebiotics is growing and an estimation for 2024 global market will reach $7.2 billion for these products (Global Market Insights 2019). However, to be considered as a prebiotic, the oligosaccharide must exhibit some criteria such as (a) not being susceptible to the action of enzymes of the gastrointestinal tract presenting resistance to the acidity of gastric juice, (b) being selectively fermented by the intestinal microflora, and (c) stimulating the growth or activity of bacteria linked to health. These substances must also exercise beneficial effects on the host health and present favorable characteristics to the manufacturing process (Wang 2009; Markowiak and Śliżewska 2018).

### 10.2.2 Mechanisms of Action

In general, the beneficial effects provided by ingesting prebiotics described in the literature (Gibson and Roberfroid 1995; Manning and Gibson 2004; Macfarlane et al. 2006; Wang et al. 2014; Sanders et al. 2019a, b) are as follows:

(a) Maintenance of the intestinal flora and increase of the fecal bolus that stimulates the intestinal transit, by the presence of fibers.
(b) Aid in the absorption and production of vitamins, such as B complex, vitamin K, and folic acid.
(c) Increased absorption of minerals, such as iron, calcium, and magnesium, decreasing the risk of osteoporosis.
(d) Decrease in cases of diarrhea, gastrointestinal, respiratory, and urogenital tract infections by stimulating probiotic bacteria and, consequently, the production of SCFAs that lead to a decrease in pH, in addition to competition for nutrients and adherence to the intestinal epithelium by pathogenic bacteria.
(e) Modulation of the immune system by the growth of probiotic bacteria responsible for the stimulation of anti-inflammatory cytokines.

(f) Decreased risk of cancer, especially of the intestinal colon.
(g) Control of glucose and cholesterol levels, which contributes to reduce cases of obesity. Prebiotics can act to decrease the pH in the cecum, which contributes to increase the excretion of bile acid; this causes the lipids stored in the liver to be required for new synthesis of bile acids, decreasing the levels of free cholesterol (Vanhoof and De Schrijver 1995; Al-Sheraji et al. 2013).

Prebiotics can also act by increasing the viscosity of the intestine, which creates a barrier that prevents the absorption of fats (Al-Sheraji et al. 2013). The control of glycemic indexes occurs through the modulation of insulin levels by a mechanism still unknown (Sousa et al. 2011).

### 10.2.3 Main Action Molecules

Prebiotics can be found naturally in milk, honey, and some vegetables such as beans, soybeans, chicory, garlic, tomatoes, bananas, leeks, onions, and asparagus (Mussatto and Mancilha 2007; Al-Sheraji et al. 2013). In the industry, prebiotics are being used as ingredients for dairy beverages, desserts, and low-calorie, low-glycemic index foods for the consumption of people with diabetes (Gibson and Roberfroid 1995; Mussatto and Mancilha 2007).

Industrially produced prebiotics need to present the appropriate daily dosage, because if ingested in excess it can cause diarrhea (Markowiak and Śliżewska 2018). Studies show that there is no prebiotic capable of stimulating a wide range of probiotics, that is, different strains of beneficial bacteria are capable of fermenting specific prebiotics, being necessary a mix of prebiotics to increase its effect on the intestinal microbiota (Moura et al. 2007; Mäkeläinen et al. 2010; Figueiredo et al. 2020).

The prebiotics that stand out in the commercialization as food supplements are lactulose, fructooligosaccharides (FOs), inulin, raffinose, mannanooligosaccharides (MOs), galactooligosaccharides (GOs), xylooligosaccharides (XOs), isomaltooligosaccharides (IMOs), and human milk oligosaccharides (HMOs) (Manning and Gibson 2004; Markowiak and Śliżewska 2018; Sanders et al. 2019a). Their chemical composition, natural sources, and main beneficial effects are summarized in Table 10.1.

#### 10.2.3.1 Fructooligosaccharides

FOs are found naturally in plants, such as garlic, onions, bananas, chicory, and tomatoes and consist of fructose units joined by β 2–1 bonds (Fig. 10.1) (Sangeetha et al. 2005; Bali et al. 2015; Sanders et al. 2019a). FOs, oligofructose, and inulin are differentiated by the degree of polymerization (dp) (Gibson and Roberfroid 1995). FOs are called oligofructose when they have dp 2 to 9; on the other hand, they are called inulin when they have a dp between 10 and 60 (Gibson and Roberfroid 1995; Cummings et al. 2001).

**Table 10.1** Chemical compositions, natural sources, and health benefits of the main prebiotics studied

| Prebiotic | Composition | Natural sources | Health benefits | References |
|---|---|---|---|---|
| Fructooligosaccharides (FOs) | Fructose (dp 2–10) | Garlic, onions, bananas, chicory, and tomatoes | Satiety. Increasing the abundance of bifidobacteria. Prevention of allergies and infections. Related to metabolic health and minerals absorption in the bowel | Gibson et al. (2017) and Sanders et al. (2019a) |
| Xylooligosaccharides (XOs) | Xylose | Vegetables, fruits, milk, and honey | Stimulation of beneficial bacteria, reduction of blood glucose, cholesterol and pro-carcinogenic enzymes. Enhanced minerals absorption and immune-stimulation | Samanta et al. (2015) and Figueiredo et al. (2020) |
| Galactooligosaccharides (GOs) | Galactose | Human’s milk and cow’s milk | Improved minerals absorption, antipathogenic activities and immunomodulatory effects. Prevention of IBS and infections. Related to urogenital health | Gibson et al. (2017) and Young et al. (2019) |
| Mannanooligosaccharides (MOS) | Mannan | Yeast cell wall | Improved insulin response and nutrients absorption. Prevention of infections. Increasing of SCFAs | Al-Sheraji et al. (2013), Gibson et al. (2017) and Markowiak and Śliżewska (2018) |
| Isomaltooligosaccharides (IMOs) | Glucose | Starch | Prevention of infections. Increasing the abundance of *Bifidobacterium* species | Al-Sheraji et al. (2013) and Markowiak and Śliżewska (2018) |
| Raffinose | Glucose, fructose, and galactose | Vegetable seeds, lentils, peas, beans, chickpeas, mallow composite, and mustard | Improving the growth of *Bifidobacterium* and *Lactobacillus* | Martíez-Villaluenga et al. (2005) and Al-Sheraji et al. (2013) |

(continued)

**Table 10.1** (continued)

| Prebiotic | Composition | Natural sources | Health benefits | References |
|---|---|---|---|---|
| Human milk oligosaccharides (HMOs) | Glucose, galactose, *N*-acetylglucosamine (GlcNAc), L-fucose, and sialic acid (*N*-acetylneuraminic acid) | Human milk | Stimulation of bifidobacteria growth in breast-fed infants. Preventing the adhesion of pathogens | Gibson et al. (2017) and Sanders et al. (2019a) |
| Inulin | Fructose (dp 10–60) | Garlic, onions, bananas, chicory, and tomatoes | Related to metabolic health. Improvement in minerals absorption. Prevention of constipation and inflammatory bowel diseases | Gibson et al. (2017) |
| Lactulose | Galactose and fructose | Lactose (milk) | Stimulation of beneficial bacteria. Prevention of inflammatory bowel diseases | Al-Sheraji et al. (2013) and Gibson et al. (2017) |

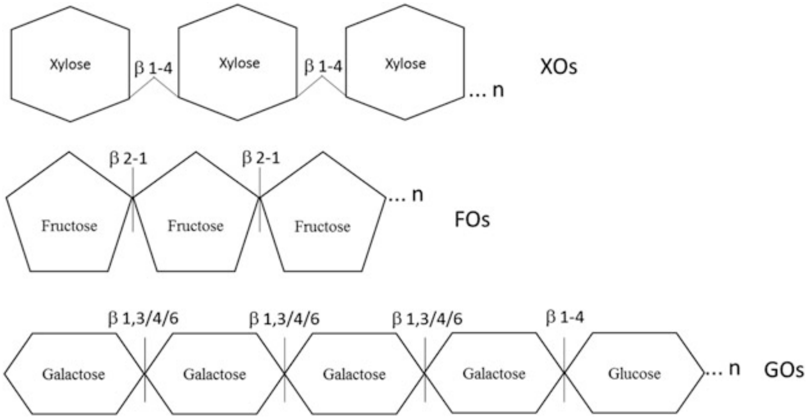

**Fig. 10.1** Schematic structures of xylooligosaccharides (XOs), fructooligosaccharides (FOs), and galactooligosaccharides (GOs)

Inulin can be obtained directly from vegetables by hydrothermal treatment, while oligofructose can be obtained through inulin or through sucrose by the action of the enzyme β-D-fructofuranosidase (Bali et al. 2015; Sanders et al. 2019a; De la Rosa et al. 2019).

The caloric value of oligofructose and inulin is estimated between 1.5 and 2 Kcal/g, and because it provides low caloric value, since they are rarely hydrolyzed by digestive enzymes, it can be included in food used by diabetics (Roberfroid 1999; De La Rosa et al. 2019). In vivo studies have shown that ingestion above 20 g/day can promote abdominal discomfort and diarrhea and consumption of only 2 to 10 g/day is sufficient to stimulate the growth of probiotic bacteria and maintain intestinal balance (Bouhnik et al. 1999; Rivero-Urgell and Santamaria-Orleans 2001; Al-Sheraji et al. 2013).

Among the functional properties of FOs, the potential to control glucose and cholesterol levels stands out (Sousa et al. 2011). These oligosaccharides have a sweet taste about 50% lower than sucrose, are considered low-calorie products, with anticariogenic properties, and do not have genotoxicity and mutagenicity. For these reasons, they are marketed as dietary and low-calorie sweeteners (Biedrzycka and Bielecka 2004).

FOs reach the intestine and selectively stimulate the growth of bacteria of the genera *Bifidobacterium*, in addition to *Lactobacillus* and some *Streptococcus*, which, by competition, inhibit the growth of putrefactive bacteria, such as those of the genera *Clostridium*, *Salmonella*, *Shigella*, *Listeria*, and *Campylobacter* (Crittenden and Playne 1996). Mäkeläinen et al. (2010) and Figueiredo et al. (2020) tested the inhibitory effect of FOs (Beneo, Belgium) on *Salmonella* growth, where practically no growth in the medium containing FOs was possible to observe, indicating a possible inhibition of *Salmonella* growth by these oligosaccharides.

Studies indicate that FOS also contribute to the absorption of minerals (calcium and magnesium) in the intestine (Roberfroid 2002; Bornet et al. 2002).

Supplementing the diet with FOs stimulated the decrease in blood lipid rates, probably due to the production of fatty acids by the fermentation of FOs by probiotic bacteria (Roberfroid 2002; De La Rosa et al. 2019).

#### 10.2.3.2 Xylooligosaccharides

XOs are nondigestible oligosaccharides found in vegetables, fruits, milk, and honey and are composed of xylose units joined by β 1–4 bonds (Fig. 10.1), which can have different branches, such as α-D-glucopyranosyl uronic acid, 4-*O*-methyl derivative, acetyl groups, or arabinofuranosyl residues (Amorim et al. 2019). XOs are marketed as a white powder and their composition and stability basically depend on the extraction process used, in addition to the types of bonds and residual sugars (Carvalho et al. 2013).

The industrial production of xylooligosaccharides is carried out using lignocellulosic materials (LCMs), such as corn cob, rice husks, barley straw, tobacco, cotton stalks, sunflower stems, wheat straw, and sugar cane bagasse (Carvalho et al. 2013). XOs can be obtained directly by acid hydrolysis and subsequent purification (Otieno and Ahring 2012), or by using acid, alkaline pretreatments, or auto-hydrolysis to extract hemicellulose (Carvalho et al. 2013; Figueiredo et al. 2017). The hydrolysis of hemicellulose for the production of XOs is usually performed by acid hydrolysis or enzymatic treatment using xylanases (Carvalho et al. 2013).

In comparison with FOs, XOs have some advantages over commercial production, as they demonstrate greater resistance to wide pH ranges (2.5 to 8) and stability at high temperatures (above 100 °C) (Amorim et al. 2019).

The recommended daily consumption for healthy adults is on average 8 to 12 g/day (Samanta et al. 2015). However, Finegold et al. (2014) evaluated that the intake of only 1.4 g/day of XOs is sufficient to increase the number of bifidobacteria present in the intestine without increasing the levels of constipation and diarrhea when compared to the group that did not ingest XOs. The maximum tolerated dose for XOs consumption by humans is 12 g/day, which can cause side effects such as nausea, flatulence, diarrhea, and distension of the abdominal region (Xiao et al. 2012; Samanta et al. 2015).

XOs also showed a possible inhibitory effect on *Salmonella typhimurium* proliferation, as low growth was observed mainly in the first hours in media containing XOs with dp 2 (xylose) (Trademark Longlive, China) (Mäkeläinen et al. 2010; Figueiredo et al. 2020).

Another trend towards the use of XOs is linked to animal feed in substitution to antibiotics, since the excessive use of these drugs can induce the resistance of bacteria, including pathogenic ones (Carvalho et al. 2013).

Many studies indicate the ability of XOs to stimulate the growth of bacteria of the genus *Bifidobacterium* and *Lactobacillus*, inhibiting and/or decreasing the proliferation of pathogenic bacteria in the intestine (Rycroft et al. 2001; Crittenden et al. 2002; Gullón et al. 2008; Mäkeläinen et al. 2010; Chen et al. 2016).

Ingestion of XOs is linked to the prevention of diabetes, cholesterol, and colon inflammation (Amorim et al. 2019). Because it has a sweet taste and having low calories, XOs can be consumed by patients with diabetes or on diets with restricted calories (Samanta et al. 2015).

Studies indicate that supplementing foods with XOs improves intestinal functions, such as calcium absorption, providing positive effects on the immune and cardiovascular system and triggering anti-allergic and anti-inflammatory activities (Grootaert et al. 2007; Chung et al. 2007; Aachary and Prapulla 2009).

#### 10.2.3.3 Galactooligosaccharides

GOs are oligosaccharides found naturally in human milk, and also in bovine milk; they are composed of galactose units joined to lactose by β bonds (Fig. 10.1) (Al-Sheraji et al. 2013; Ferreira-Lazarte et al. 2019; Young et al. 2019). It has a sweetening power of 0.3 to 0.6 times in relation to sucrose (Torres et al. 2010).

GOs are obtained from the action of β-galactosidases using lactose as a substrate; depending on the origin of the enzyme, different mixtures of GOs can be formed (Botvynko et al. 2019). The consumption of 10 g/day is adequate to balance the intestinal flora, although some authors claim that the consumption of 2 to 3 g/day is already sufficient to increase the levels of *Bifidobacterium* in the intestine (Torres et al. 2010; Sousa et al. 2011; Al-Sheraji et al. 2013). The maximum tolerated dose is around 0.3 to 0.4 g/kg of the consuming individual (Sako et al. 1999).

Studies indicate that diets enriched with GOs positively affected the composition of the intestinal flora, such as the increase in the number of *Bifidobacterium* and *Lactobacillus* in the intestine (Searle et al. 2009; Torres et al. 2010).

"In vitro" tests with tissue cultures simulating the intestinal environment showed that the presence of GOs avoided adhesion and invasion by *Salmonella typhimurium*, preventing colonization by this type of pathogen (Searle et al. 2009). The inhibitory effect of GOs (Danisco) on the growth of *Salmonella typhimurium* was evaluated by an "in vitro" test, where Mäkeläinen et al. (2010) observed an inhibition of *Salmonella typhimurium* growth for this prebiotic.

GOs also act as a prebiotic in patients with IBS, stimulating the activity of *Bifidobacterium* in the intestine and, consequently, relieving the symptoms of the disease (Silk et al. 2008). The intake of GOs also helps in the absorption of mineral salts, mainly calcium, and is related to the reduction of toxic metabolites produced by pathogens and an increase in lactose tolerance (Sousa et al. 2011; Young et al. 2019).

Because of the beneficial effects, GOs have been a frequent ingredient added to foods, even used as a possible complement of human milk for infants (Botvynko et al. 2019).

In general, the study of different prebiotics and their methods of action are important factors in understanding their influence on the composition of the intestinal microbiota.

## 10.3 Intestinal Microbiota

The gastrointestinal tract is intensely colonized by several microorganisms, presenting a complex and dynamic interaction between different populations of bacteria, fungi, archaea, and viruses (Wang et al. 2017; Tang et al. 2019). This community of microorganisms that inhabit the gut is often called a "microbiota." The microbiota, also called microbiome, is constituted of approximately 10 trillion microorganisms, presenting from 300 to 500 species covering around two million genes (Quigley 2010; Tang et al. 2019).

### 10.3.1 Composition and Colonization of the Microbiota

Colonization of the intestine occurs during the birth process, as part of the microbiota is derived from the mother to the newborn (Maslowski and Mackay 2011). Some factors are essential to determine the composition of the intestinal microbiota such as the type of delivery, breastfeeding, environmental factors, and the use of antibiotics during the first days of life (Derrien et al. 2019).

In general, the gastrointestinal tract is inhabited by microorganisms along its entire length; however, the colon has a greater colonization of bacteria. The phyla of microorganisms most frequently found in the intestines of adult individuals are Bacteroidetes, Firmicutes, Actinobacteria, Proteobacteria, and Verrucomicrobia (Guarner and Malagelada 2003; Tang et al. 2019).

In-depth analysis of the microbiota composition requires detailed techniques for the cultivation of bacteria in different growth media and methods for taxonomic identification of the isolates (Guarner and Malagelada 2003). In humans, there are some prominent genera such as *Bacteroids*, *Bifidobacterium*, *Eubacterium*, *Clostridium*, *Peptococcus*, *Peptostreptococcus, Prevotella*, and *Ruminococcus* (Guarner and Malagelada 2003; Derrien et al. 2019). In addition, other genera can be frequently found, such as *Escherichia*, *Enterobacter*, *Enterococci, Klebsiella*, *Lactobacillus*, and *Proteus* (Guarner and Malagelada 2003).

The type of diet, lifestyle, geography, use of antibiotics, and infections can determine the variation in genera found in different individuals. For example, a diet rich in fiber may be associated with a greater diversity of the microbiota, as well as a diet rich in fats, very common in developed countries, is correlated with an increase in *Bacteroides* and a decrease in *Prevotella* and *Succinivibrio* abundance (Derrien et al. 2019). Age is also an important factor. In healthy children, the intestinal microbiota has a different composition when compared to adults because it tends to develop slowly; in the earlier stages of life *Bifidobacterium* spp. are very abundant and show a reduction in their number in the adult phase (Derrien et al. 2019).

### 10.3.2 Importance of Intestinal Microbiota

Colonization of the intestinal tract by specific types of bacteria has some benefits for the host health. The microbiota plays an important role in nutrition and nutrient absorption, in the stability of the intestinal epithelial protection barrier against pathogens, and in the development of the immune system (Russel et al. 2011; Guarner and Malagelada 2003; Tang et al. 2019). The metabolic function of the intestinal flora is related to the fermentation of carbohydrates that escape the action of enzymes and gastric juice present in the digestive system. Such function results in the main source of energy in the form of fatty acids available in the colon, and also in improving the absorption of ions by the host's intestinal epithelium (Gibson and Roberfroid 1995; Wang et al. 2017). The microbiota is also involved in the production of vitamins, mainly vitamin K, responsible for blood clotting (Guarner and Malagelada 2003; Quigley 2010).

The formation of short-chain fatty acids (SCFAs) (acetate, propionate, and butyrate), during the fermentation of the microbiota, provides the host with benefits linked to the control of the differentiation and proliferation of intestinal epithelial cells, preventing the formation of neoplastic cells, being key in preventing colon cancer (Sanders et al. 2018; Tilg et al. 2018). The balanced intestinal flora helps keep the intestinal epithelium intact, which may represent one of the barriers against the invasion of pathogens. In addition, the roles of the microbiota against microorganisms related to infections may also occur through competition for nutrients and adhesion sites present in the intestine, through the decrease in pH as a result of the production of acids by the fermentation of carbohydrates, and finally through the release of bacteriocins (Guarner and Malagelada 2003; Leahy et al. 2005).

### 10.3.3 Microbiota and Diseases

Dysbiosis in the intestinal microbiota, a condition of microbial community imbalance, is strongly associated with the appearance of diseases, mainly infections (Tang et al. 2019; Wang et al. 2017). Some situations directly affect intestinal balance: changes in eating habits, stressful situations, usage of antibiotics, environmental changes; all may lead to an increase in the number of pathogenic microorganisms. Colonization by pathogens generates important anti-inflammatory responses, and treatments for these types of infections can also lead to a very large change in the composition of the microbiota. The excessive proliferation of the group of pathogenic bacteria may cause the host disturbances like diarrhea, infections, release of toxic or carcinogenic substances, and even pathologies related to the immune system, as, for example, autoimmune diseases and allergies (Gibson and Roberfroid 1995; Johannsen and Prescott 2009).

Disturbances in the intestinal microbiota are the main cause of antibiotic-associated diarrhea (AAD), a common complication in hospitalized patients undergoing antimicrobial therapy (Velasco et al. 2018). Infections with *Clostridium* *difficile* are often associated with AAD, where dysbiosis caused by antibiotics leads to a sharp drop in resistance to toxins produced by *C. difficile*, enabling its rapid infection (Wang et al. 2017).

Many species of *Salmonella enterica* can induce gastrointestinal diseases known as salmonellosis, caused by the ingestion of contaminated water or food. After intestine colonization by *Salmonella*, the cells of the intestinal epithelium are attacked causing changes in the microvilli, which provokes a reduction in the enzymatic activities of the brush border (Symonds et al. 2012). In this way, some intestinal functions are affected, for example, the absorption of ions, which results in diarrhea (Symonds et al. 2012).

Colon cancer is also involved in the imbalance of intestinal flora. A diet rich in fats and red meats, mainly processed food and high body weight, significantly affects the microbiota metabolic activity and composition (Tilg et al. 2018). The anaerobic metabolism of peptides and proteins by some proteolytic bacteria can generate toxic substances such as ammonia, amines, and phenols. These compounds are known as colon cancer initiators or promoters (Gibson and Roberfroid 1995; Guarner and Malagelada 2003). Bacteria of the genus *Clostridium* have been associated with an increased incidence of colon cancer and tumors (Tilg et al. 2018).

Metabolic disorders are also related to intestinal microbiota dysbiosis, such as type 2 diabetes and obesity. Research has intensified in order to assess how food factors directly influence the population of microorganisms that inhabit the intestine, and concludes that diet modulates the composition and function of the microbiota (Wang et al. 2017). A microbiota with altered diversity and resilience was found as a common characteristic among patients with type 2 diabetes; for the reason it can alter the metabolism and induce insulin resistance, for example (Wang et al. 2017).

The manipulation of intestinal microbiota for the treatment of ulcerative colitis and other gastrointestinal diseases has been shown to be very advantageous; however, regarding Crohn's disease, there is little evidence that this approach can act to induce remission of the disease and studies in this area are still inconclusive (Limketkai et al. 2020).

Cardiovascular diseases, anxiety symptoms, allergic sensitivities, asthma, and eczema may be more effective in treatments when used together with ingredients that regulate the intestinal microbiota (Tang et al. 2019; Yang et al. 2019; Zimmermann et al. 2019). These studies have contributed to the knowledge that a good balance of the intestinal flora can contribute to prevention and even a possible treatment associated with the existing treatments for certain diseases.

The use of antibiotics, a common practice in the treatment of these types of diseases, has aroused the concern of researchers and the medical community due to the risk of inducing resistant strains and AAD. For this reason, research has been carried out to seek the replacement of antibiotics with treatments with beneficial bacteria (probiotics) (Guarner and Malagelada 2003; Velasco et al. 2018; Tilg et al. 2018).

The evident importance of the intestinal microbiota corroborates the great interest in the development of foods that preserve or stimulate the growth of probiotic microorganisms.

## 10.4 Probiotics

### 10.4.1 Definition and Classification

In 1965, Lilly and Stillwell presented the first definition of probiotics referring to substances produced by microorganisms related to promoting the growth of other microorganisms. The widely quoted Food and Agricultural Organization, of the World Health Organization, defined and recognized the benefits of probiotics in 2001. Currently, this definition has been revised and probiotics are described as living microorganisms that, when ingested in adequate amounts, are related to the balance of intestinal flora and the well-being of the host (Hill et al. 2014). The growing interest in the use of probiotics, mainly in the food industry for food supplementation, makes this ingredient of high added value, with an estimated value in the probiotics market of above $69.3 billion in 2023 (Markets and Markets 2019).

In order to be classified as suitable and safe for consumption, it is extremely important that the microorganism is taxonomic identified; preferably of human origin; is able to survive in the intestinal colon; resists acid pH, enzymes, and bile salts; colonizes the intestine; is not pathogenic; and does not release toxins, Showing antagonism to pathogens, bringing benefits to the host, and remaining viable throughout industrial processes as well as during the period of use and storage are also important characteristics (Plaza-Diaz et al. 2019; Sanders et al. 2019a).

It is very important to ensure safety in the use of probiotics, since their mechanisms of action are not yet fully understood.

### 10.4.2 Mechanisms of Action

The mechanisms of action by which probiotics play their beneficial role are known through “in vitro” tests, cell cultures, humans, and other animal models. However, in clinical circumstances these benefits are not yet fully understood (Sanders et al. 2019a). Current knowledge shows that probiotics can beneficially influence beyond the colonizing microbiota and their mechanisms of action depend on several factors, such as the types of microorganisms present in the intestine and the ability of the probiotic to act according to the host’s needs (Sanders et al. 2019b). Probiotics can have several mechanisms of action in a single strain and the mode and spectrum of action of these mechanisms can also vary between different strains (Sanders et al. 2019b). The probiotics mechanisms of action are summarized in Fig. 10.2.

#### 10.4.2.1 Modulation of the Immune System

Probiotics are related to the modulation of the immune system by stimulating the production of anti-inflammatory molecules. The probiotic interacts via receptors in the intestinal mucosa regulating the production of antibodies, phagocytes, and natural killer cells (Sanders et al. 2019b). These microorganisms can increase the levels of anti-inflammatory cytokines and reduce production of pro-inflammatory

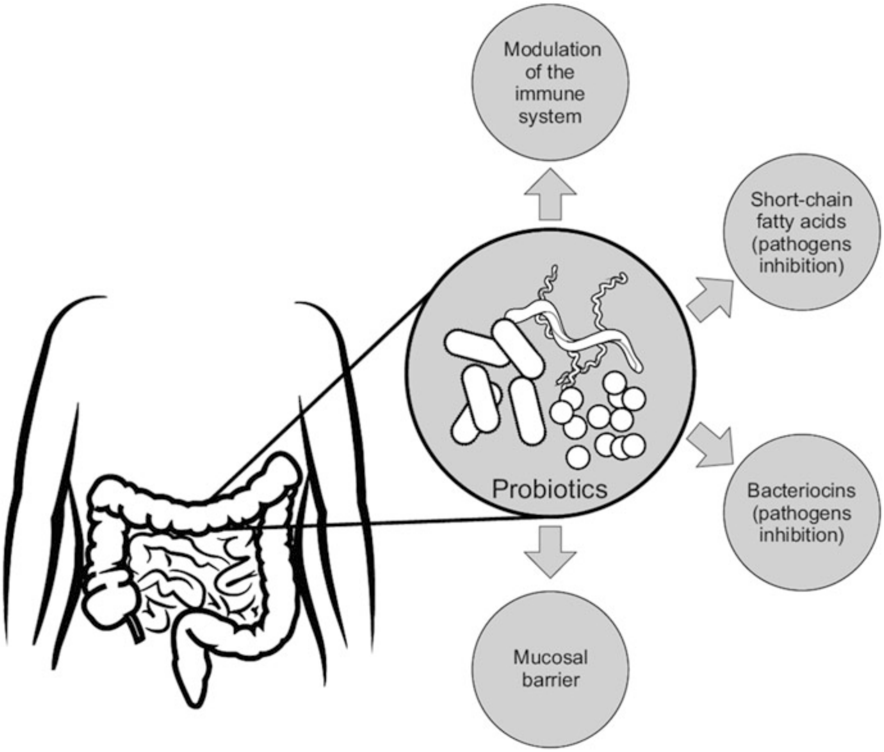

**Fig. 10.2** Probiotics mechanisms of action

cytokines in the intestine; this regulatory system decreases the incidence of colon cancer and colitis (Sanders et al. 2019b; Plaza-Diaz et al. 2019). Some studies show that the regulation of the system can suppress chronic inflammation, presenting beneficial effects for the treatment of irritable bowel syndrome (IBS) (Quigley and Flourie 2007; Wasilewski et al. 2015; Quigley 2019).

#### 10.4.2.2 Mucosal Barrier

The intestinal mucosa barrier is very important for the individual's health, as it presents selective permeability allowing the entry of some nutrients (Sanders et al. 2019a). The intestinal mucosa is also responsible for secreting mucins, proteins that prevent the adhesion of pathogens on epithelial cells (Plaza-Diaz et al. 2019). The adhesion of probiotics provides an improvement in the mucosal barrier, as they stimulate a greater production of intestinal epithelial cells and protective substances, such as mucin (Sanders et al. 2019a).

#### 10.4.2.3 Inhibition of Pathogens

Probiotics act in inhibiting pathogens due to their important role in the mucosal barrier of the intestine as discussed in the previous item. Furthermore, these microorganisms can compete for nutrients and adhesion sites present in the intestine, preventing the proliferation of pathogens (Sanders et al. 2019b). The production of short-chain fatty acids (SCFAs) and bacteriostatic or bactericidal substances, such as bacteriocins, is being widely studied as the main competitive exclusion mechanism for invading microorganisms from the natural microbiota (Nagpal et al. 2018; Sanders et al. 2018).

#### 10.4.2.3.1 Short-Chain Fatty Acids (SCFAs)

Organic acids are the main end products from the carbohydrate metabolism of some probiotic bacteria, mainly *Bifidobacterium* and *Lactobacillus* (Sanders et al. 2019b). SCFAs including lactic, butyrate, acetic, and formic acids have a great inhibitory potential of microorganisms that cause important infections, mainly Gram-negative bacteria (Sanders et al. 2018).

The undissociated forms of these organic acids passively pass through the bacterial cell wall of the pathogen and dissociate (Vieco-Saiz et al. 2019). The decrease in pH in the cytoplasm, or the accumulation of the ionized form of the acid inside the bacteria, promotes its death, since it modifies the proton gradient and the electric charge in relation to the extracellular medium, inhibiting its metabolic functions (Carpenter and Broadbent 2009).

This hypothesis implies that there would be a change in the transport of amino acids and phosphates, in addition to inactivating endogenous enzymes in the cell (Carpenter and Broadbent 2009). In addition, it causes an increase in the osmotic pressure of the cell due to the electrical charge, since there would be an increase in the concentrations of sodium and potassium (Carpenter and Broadbent 2009). In this way, an intracellular ionic force is created that promotes the disruption of the microorganism's cell wall.

Among the classes of acids, weak ones are more efficient at penetrating and acidifying the interior of the cell than strong acids, due to their dissociation capacity (Wang et al. 2014).

#### 10.4.2.3.2 Bacteriocins

Bacteriocins are peptide compounds derived from the ribosomal synthesis of some bacteria and secreted in the extracellular environment, which have antimicrobial effects (Vieco-Saiz et al. 2019; Gao et al. 2019).

Due to its bactericidal or bacteriostatic effect, it has often been used in the food industry as a natural preservative to replace chemical preservatives (Salman et al. 2020). Bacteriocins have been studied as a possible complement for treatments of infections or even as an alternative to the use of antibiotics, since in contrast to the latter, bacteriocins act in certain species without affecting the composition of the microbiota (Vieco-Saiz et al. 2019).

The classification of bacteriocins takes into account characteristics such as structure, mode of action, size, antimicrobial potential, immunity mechanism, and target cell receivers (Salman et al. 2020).

Cotter et al. (2005) presented a classification that divides these molecules into classes, as follows:

Class I: Lantibiotics, that is, bacteriocins that have the amino acid lanthionine that can be further subdivided into two types A and B. They are small and thermostable peptides whose molecular weight is less than 5 kDa. The classic example of this class is Nisin, produced by strains of *Lactococcus lactis*, usually isolated from dairy products. It is the most studied and accepted bacteriocin in the food industry.

Class II: These are bacteriocins that do not have lanthionine, thermostable, small (<10 kDa). They have a large concentration of small amino acids such as glycine and are cationic and amphiphilic, culminating in its great ability to permeabilize membranes. They are produced by a wide variety of species, including *Enterococcus* and *Lactobacillus.* They can be subdivided into four subgroups: IIa (Pediocin-like bacteriocins), IIb (Bacteriocins from two peptides), IIc (Cyclic bacteriocins), and IId (Linear bacteriocins that are not pediocin).

Class III: They are larger (> 30 kDa) and thermolabile compounds. They were identified predominantly among the genus *Lactobacillus*. Unlike the other groups, these bacteriocins are sensitive to high temperatures, being inactivated in the range of 60–100 °C in heat treatment that lasts from 10 to 15 min.

The bacteriocins of the first two groups are those of greatest technological interest due to their greater applicability in industrial processes and their greater abundance.

### 10.4.3 Probiotic Properties of *Bifidobacterium* and *Lactobacillus*

*Bifidobacterium* and *Lactobacillus* are genera of facultative anaerobic Gram-positive bacteria, often found in the colon and commonly associated with health of the host (Leahy et al. 2005; Makras and De Vuyst 2006). Both genera are commonly considered as probiotics.

These bacteria are saccharolytic; they ferment carbohydrates from the host's food, in addition to having no pathogenic representatives (Macfarlane et al. 2006; Quigley 2010).

The population number of probiotic bacteria in the intestine is relatively high, around $10^7$–$10^{10}$ CFU × $g^{-1}$; this number can vary according to the individual's age, use of antibiotics, and diet (Makras and De Vuyst 2006; Markowiak and Śliżewska 2018; Nagpal et al. 2018).

A study using meta-analysis of probiotic strains such as *Saccharomyces boulardii* and *Lactobacillus rhamnosus* GG showed efficiency of these strains in preventing AAD (McFarland 2006). So far, these two probiotic strains are the only ones that have been shown to be efficient in the treatment of AAD (Velasco et al. 2018).

Some studies indicate that *L. rhamnosus* GG, *L. plantarum*, *L. acidophilus*, *L. paracasei*, *B. animalis*, *B. lactis*, *B. breve*, and *B. longum* are able to alleviate the symptoms of inflammatory bowel disease, such as bloating, diarrhea, and nutritional deficiencies (Coqueiro et al. 2018).

"In vivo" studies show that *Bifidobacterium infantis* 35,624 attenuated the levels of infection in the brush-border enzymatic activities caused by *Salmonella*, probably due to the modulation of the host's immune system (Symonds et al. 2012; Scully et al. 2013). Ren et al. (2013) demonstrated that strains such as *L. salivarius* and *L. plantarum* had the potential to prevent inflammatory diseases, including those caused by *Salmonella typhimurium*.

Related to colorectal cancer, *L. rhamnosus*, *B. lactis*, *B. longum*, *L. helveticus*, and *L. acidophilus* can act to reduce the formation of tumors and inflammatory responses, in addition to reducing the effects of cytotoxic and genotoxic, ammonia concentration, β-glucosidase, and oxidative stress (Eslami et al. 2019).

Many products have been commercialized for many years containing probiotics as food supplements, mainly in fermented drinks, such as *L. acidophilus*, *L. casei*, *L. delbrueckii*, *L. plantarum*, *L. rhamnosus*, *B. adolescentis*, *B. bifidum*, *B. longum*, *B. infantis*, *B breve*, *B. lactis*, and *B. animalis* (Gibson and Roberfroid 1995; Holzapfel et al. 1998).

## 10.5 Symbiotics

Symbiotics consist of a combination of probiotic microorganisms and prebiotic ingredients. Gibson and Roberfroid (1995) defined symbiotics as a "mixture of probiotics and prebiotics that beneficially affects the host by improving the survival and implantation of live microbial dietary supplements in the gastrointestinal tract, by selectively stimulating the growth and/or by activating the metabolism of one or a limited number of health-promoting bacteria, and thus improving host welfare."

The mechanisms of action and criteria for the selection of symbiotics are the same studied in probiotics and prebiotics (Markowiak and Śliżewska 2018). Symbiotics production can take two different approaches according to the prebiotic chosen to compose the product (Kolida and Gibson 2011; Sanders et al. 2019a). It can be considered "complementary," where the prebiotic choice has no relation with the probiotic of the elaborated product, or it can be considered "synergistic," when the prebiotic is chosen specifically to stimulate and guarantee the survival of the selected probiotic (Kolida and Gibson 2011; Sanders et al. 2019a).

Because they present different approaches, each "complementary" and "synergistic" symbiotic shows different formulations according to their purpose. For example, in the first approach, the target of the prebiotic is to cause health benefits to the host by maintaining the balance of the intestinal flora, regardless of the probiotic selected (Kolida and Gibson 2011). Therefore, this symbiotic composition generally presents high concentrations of prebiotics to obtain the desired purpose (Kolida and Gibson 2011). In the "synergistic" approach, the prebiotic's target is to guarantee the survival and implantation of the probiotic that makes up the product; in this case, the prebiotic concentration may be lower, as long as it fulfills the proposed effect (Kolida and Gibson 2011).

Some studies show the effect of symbiotic ingestion on the intestinal microbiota. Morelli et al. (2003) analyzed the feces of 12 healthy adults and demonstrated that the combination of inulin, *Lactobacillus paracasei* and *Lactobacillus gasseri*

($0.5 \times 10^9$ CFU—colony-forming units) ingested for 15 days increased the populations of *Lactobacillus* and *Bifidobacterium* in the intestine.

A study of 51 healthy elderly people ingesting a symbiotic containing *L. acidophilus* ($2 \times 10^9$ CFU) with 5 g of lactitol demonstrated by real-time PCR tests an increase in the populations of *Lactobacillus* and *Bifidobacterium* (Ouwehand et al. 2009). The combination of XOs and *Bifidobacterium lactis* can confer additional benefits to the intestinal microbiota and the immune system, due to the increased survival of live bacteria present in the food supplement (Childs et al. 2014).

Studies with commercial symbiotics, Flortec (Bracco Co), which contains *L. paracasei*, XOs, glutamine, and arabinogalactan, and Zir Fos®, which contains *B. longum* and FOs, have shown efficiency in reducing symptoms, such as pain and diarrhea, of patients with irritable bowel syndrome (Dughera et al. 2007; Adriulli et al. 2008).

Symbiotic products are also related to decreased risk of colon cancer, as the daily consumption of fibers associated with the maintenance of intestinal flora plays a fundamental role in the proper functioning of cell division, preventing the formation of tumor cells (Quigley 2019). Le Leu et al. (2005) evaluated the combination of resistant starch with strains of *B. lactis* and *L. acidophilus*, alone or in mixtures, and observed an increase in *Lactobacillus* and *Bifidobacterium*, in addition to the combination of starch and *B. lactis* increasing the acute apoptotic response of tumor cells.

The interest in the development and use of new symbiotics has risen due to studies that prove the benefits related to alternative treatments for intestinal diseases, in addition to its use as a preventive for such diseases, although determining the minimum concentrations of the components is still a challenge for the researchers.

## 10.6 Evaluation Models of Prebiotics, Probiotics, and Symbiotics

### 10.6.1 Prebiotics

#### 10.6.1.1 "In Vitro" Tests

Some "in vitro" methodologies are proposed to evaluate characteristics such as resistance to the action of digestive enzymes, fermentability by the intestinal flora, and, finally, the selectivity of the prebiotic by beneficial bacteria. It is very common that in these types of tests the chemical simulation of environments such as the small intestine is performed, where salivary, pancreatic, and intestinal enzymes are added and after a few hours the degradation of the oligosaccharide is evaluated (Figueiredo et al. 2020).

Often pure cultures or fecal samples are used to determine the fermentation and selectivity of prebiotics by intestinal bacteria (Kolida and Gibson 2011). Both tests have advantages and disadvantages, since in pure cultures it is not possible to identify the inhibitory effects of pathogens by the growth of probiotics; however, tests with fecal samples are not always completely conclusive in relation to the identification of the species present (Roberfroid 2007).

"In vitro" tests are very important tools to determine the efficiency and safety of prebiotics, with lesser costs, ease of handling, and without involving many ethical aspects, while "in vivo" tests are being questioned progressively. The "in vitro" tests generally provide greater predictability for the next stage that generally involves the "in vivo" tests, which are mainly aimed at observing the action of prebiotics in relation to intestinal diseases.

#### 10.6.1.2 "In Vivo" Tests

Candidates for prebiotics must pass "in vivo" tests in rats and later in humans with experiments using double-blind, control, and placebo (Kolida and Gibson 2011). A very common "in vivo" method for assessing digestibility is through oral administration of the prebiotic to rats free of infection or treated with antibiotics to suppress the intestinal flora; after this process, the feces are collected and the presence of the administered product is analyzed (Nilsson and Bjorck 1988). Some methodologies make it possible to determine digestibility in humans, after ingestion of the prebiotic. In such cases, blood tests are done to observe the increase or not of glycemic rates in the circulatory system (Molis et al. 1996; Gibson et al. 2004). The same tests are performed to assess fermentability and selectivity; however the flora is kept intact and the evaluation consists of the administration of prebiotics and subsequent measurement of the concentration of gases (mainly oxygen) produced, or performed by collecting fecal samples and analyzing the amount of prebiotics recovered in feces after oral administration (Gibson et al. 2004; Roberfroid 2007). Molecular biology tools can also be used to study the growth stimulation of beneficial bacteria in the intestine by ingesting prebiotics (Kolida and Gibson 2011).

The low number of individuals in "in vivo" studies with patients with gastrointestinal diseases impairs the reliability and interpretation of results (Kolida and Gibson 2011).

### 10.6.2 Probiotics

#### 10.6.2.1 "In Vitro" Tests

For the evaluation of probiotics by "in vitro" tests, it is important that they are characterized as safe for human consumption. Thus, many commercialized probiotics are isolated from the gastrointestinal tract of humans, as they do not present risks to human health, in addition to being more effective in adapting to the intestinal environment (Kolida and Gibson 2011). Molecular techniques should make it possible to assess the probability of probiotic strains to acquire pathogenicity and resistance to antibiotics (Quigley 2010).

Some tests are performed to determine the resistance of probiotics to technological processes, such as durability and viability of the microorganism (Quigley 2010; Kolida and Gibson 2011). Another important step in this type of test is to determine the probiotic's ability to resist the acidity of gastric juice and simulate the intestinal environment, allowing the assessment of the ability of the microorganism to adhere to the intestinal epithelium (Kolida and Gibson 2011).

#### 10.6.2.2 "In Vivo" Tests

The "in vivo" tests of probiotics are more focused on analyzing their effects in individuals diagnosed with gastrointestinal diseases. In rats and humans, these tests ensure the efficiency of probiotics in fighting or preventing certain diseases, especially in the gastrointestinal tract (Kolida and Gibson 2011; Tong et al. 2013).

Few studies including "in vitro" or "in vivo" tests demonstrate the efficacy of mixtures of probiotic strains; moreover, the mechanism that results in synergism in terms of increased bioactivity is poorly understood (Rosenfeldt et al. 2003; Kim et al. 2003; Viljanen et al. 2005; Chapman et al. 2011, 2012). In many studies, the comparison between pure and mixed cultures is not always performed by standardizing the inoculum concentration, which can generate unreliable results (Chapman et al. 2012). Further studies are needed to define the ideal combination of probiotics, without an antagonistic effect between species, in order to expand the benefits to the host and enhance the inhibition of a greater variety of pathogens.

### 10.6.3 Symbiotics

#### 10.6.3.1 "In Vitro" and "in Vivo" Tests

The establishment of a new symbiotic formulation must pass all the "in vitro" and "in vivo" evaluation criteria for prebiotics and probiotics described above (Kolida and Gibson 2011). The components of the symbiotic formulation need to be evaluated separately to determine whether the positive effects of the symbiotic were superior to the separate ingredients (Kolida and Gibson 2011). Determining the minimum dose of each component and the storage conditions are fundamental studies for creating a new product (Kolida and Gibson 2011). Currently, few "in vivo" studies are being carried out to demonstrate the effects of symbiotic ingestion in patients with diseases that affect the intestine, although the trend is that these studies will increase over the years due to the potential that these products have in preventing certain diseases.

## 10.7 Conclusion and Future Perspectives

Many researches seek to understand the mechanisms that lead to an important relationship between the intestinal microbiota and the health of the host. The development and consumption of probiotic, prebiotic, and symbiotic ingredients have increased both in human food and in other animals. Consequently, the market for these products has grown over the years all over the world.

The next steps in research of this field aim to fully clarify the mechanisms of action in the microbiota, as well as the effect of the synergism between several prebiotics mixed with several probiotics, combined or not, in the control of specific diseases and to characterize the benefits for the health and to avoid future diseases; as a consequence, to develop new products that can reach a wide range of disease control and/or avoid future diseases, replacing the classic medicines; and in addition, to stimulate the formulation of new foods with some special ingredients (prebiotics and probiotic) which can increase the health benefits.

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# Hemicellulose Sugar Fermentation: Hydrolysate Challenges, Microorganisms, and Value-Added Products

# 11

João Paulo Candido, Carolina Freitas, Alison Andrei Schmatz, Jefferson Poles Felipuci, Dilza Aparecida Nalin de Oliveira Leite, Dejanira de Franceschi de Angelis, and Michel Brienzo

## Abstract

The efficient use of xylose represents one of the most important pillars for the economic development of converting lignocellulosic biomass into value-added by-products with potential use in various activities, such as pharmaceutical, food, or biofuel industries. The conversion of lignocellulosic biomass into bioproducts of industrial value needs to be subjected to pretreatment, enzymatic hydrolysis, fermentation, and distillation or purification step. Xylose is one of the main sugars obtained by hydrolysis of biomass hemicellulose fraction. However, xylose metabolism is restricted to a few microorganisms. This makes it difficult to establish an industrial scale of production to obtain value-added products. In addition, the use of lignocellulosic pretreatment can result in sugar degradation products: furfural (sugar pentose degradation) and 5-hydroxymethyl furfural (5-HMF) (sugar hexoses degradation); formic and levulinic acids from the degradation of furfural and 5-HMF and acetic acid from the acetyl group structures of hemicellulose; and phenolics compounds released from lignin. All of these compounds are related to losses in the fermentation process. Therefore, it is important to define the best strategies for choosing a pretreatment in order to obtain high sugar release and low conversion of contaminants. Processes that aim at detoxifying the fermentative medium must be carried out. In addition, it is necessary to establish ideal cultivation conditions, such as the concentration of

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M. Brienzo (ed.), *Hemicellulose Biorefinery: A Sustainable Solution for Value Addition to Bio-Based Products and Bioenergy*, Clean Energy Production Technologies, https://doi.org/10.1007/978-981-16-3682-0_11

dissolved oxygen and pH regulation of the médium, which controls that lead to better xylose conversion rates. Studies have been conducted with potential pentose fermenting microorganisms, such as *Scheffersomyces stipitis, Spathaspora hagerdaliae, Candida shehate* (ethanol production); *Meyerozyma guilliermondii; Spathaspora passalidarum* (xylitol production); *Klebsiella oxytoca; Klebsiella pneumonia; Bacillus licheniformis* (2,3-butanediol (BDO) production). Therefore, research should be focused on genetic changes in yeast strains, for the production of high-value compounds as ways to establishing gains of the biofuels production, chemicals, and food. This chapter discusses the main implications involving the conversion of hemicellulose sugar into value-added products and the main microorganisms used in these processes.

**Keywords**

Lignocellulosic biomass · Xylose fermentation · Value-added products

## 11.1 Introduction

Biomass originated from various industrial or food production processes (agricultural and agro-industrial by-products) is an important source of carbohydrates (Rastogi and Shrivastava 2017). These materials can be used in bioprocesses to obtain inputs used in activities such as the pharmaceutical and food industries (Forster-Carneiro et al. 2013). Among the main biomasses for obtaining value-added products, it can be mentioned those coming from sucrose and amylaceous materials, like bagasse from sugarcane in Brazil and corn stover in the USA. Other sources include rice straw, wheat straw, forestry waste, fruit and vegetable waste, among others (Chandel et al. 2018).

The use of lignocellulosic material in industrial bioprocesses depends on its chemical constitution. The typical constitution of lignocellulosic material is formed by cellulose, hemicellulose, and lignin (Antunes et al. 2018). The molecular composition of this material is variable (40–60% cellulose, 20–40% hemicellulose, and 10–25% lignin) (Kang et al. 2014) and depends on the type and origin of the biomass (Brienzo et al. 2014). Among these constituents, there is great interest in the utilization of hemicellulose due to its properties and heterogeneity (Brienzo et al. 2016a).

Hemicellulose is a polysaccharide formed by hexoses (C6 sugar) (D-glucose, D-galactose, and D-mannose), pentoses (C5 sugar) (D-xylose, and L-arabinose) (Rastogi and Shrivastava 2017; Van Der Pol et al. 2014; Gírio et al. 2010) and also present of acetyl substituents (Saha 2003). Acetic acid, which is an important inhibitor of fermentation processes, is originated from this last group (Perna et al. 2018).

Hemicellulose differs substantially from cellulose because part of its structure is amorphous, this characteristic facilitates the hydrolysis of hemicellulose when compared to cellulose (Rastogi and Shrivastava 2017). The depolymerization of hemicellulose must be associated with a pretreatment that can release its monomers, especially xylose (Zheng et al. 2009). Among the most applied pretreatments for depolymerization of hemicellulose is the use of diluted acids and steam explosion (Chandel et al. 2018). Such treatments (methods are not selective) allow the release of sugar. On the other hand, a part of them is transformed into intermediate compounds that are often described as inhibitors of microbial metabolism, damaging the fermentative yield (Mussato and Roberto 2004). Therefore, a detoxification step is often required after the pretreatment process. In the detoxification process a physical, chemical, and biological methods can be employed, associated or not. Such methods are used to decrease or eliminate the concentration of compounds formed by the degradation of sugar during the depolymerization stage of hemicellulose. After the detoxification steps, the recovered liquid fraction can be used to obtain products of interest by fermentation.

The fermentation of xylose does not achieve desirable fermentation yields (Prior et al. 1989; Chandel et al. 2018). Therefore, the microbial conversion of hemicellulose (mainly xylose) biomass into value-added products is considered an interesting step for the utilization of lignocellulose materials (Milanez et al. 2015; Gírio et al. 2010; Lamounier et al. 2020). Monomers obtained from hemicellulose can be transformed into value-added products through fermentation or non-fermentative processes. This chapter discussed value-added products obtained through fermentation using xylose, such as xylitol, ethanol, butanediol. Pretreatment methods were reported as the effect on the hydrolysate produced, and effort on the microorganism screening and development to support the inhibitors compounds.

## 11.2 Value-Added Products from Hemicellulose

Lignocellulosic materials constitute an important alternative feedstock for bioenergy production (Haldar and Purkait 2020). This is due to the abundance of the by-products derived from agricultural and agro-industrial processes. The hemicellulosic fraction after hydrolysis can be fermented for the xylose utilization (McMillan 1993; Martins et al. 2018) and through various metabolic routes it can be converted into ethanol, xylitol, and biopolymers (Canilha et al. 2013; Chandel et al. 2018).

Xylose, a sugar derived from hemicellulose is one of the most widely available carbohydrates in nature, so there is a great biotechnological potential to convert it into various products of interest (Fig. 11.1). Some microorganisms can metabolize the five-carbon sugar naturally or by metabolic engineering modifications and transform it into other compounds. The main products obtained from xylose fermentation are bioethanol and xylitol, however, some chemicals can also be produced (Zhao et al. 2020).

Currently, xylitol is still the largest market for the xylose converting process. It was discovered in 1890 by the German scientist Emil Fisher and its commercialization as a sweetener became interesting during the shortage of sugar in World War II. There is no petrochemical alternative to obtain xylitol, it can only be produced from biomass. Xylitol is considered a chemical platform molecule, which means that

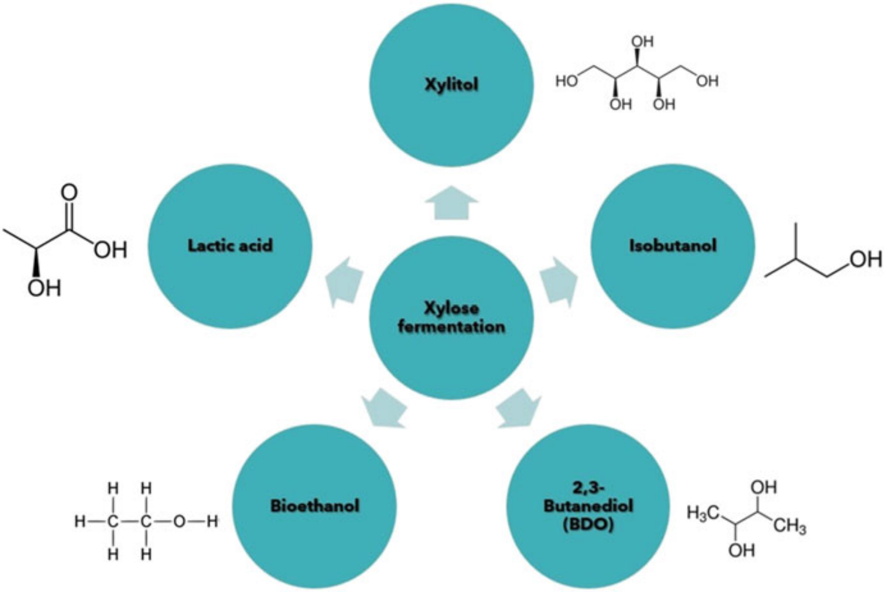

**Fig. 11.1** Products from xylose fermentation

it has the capacity to be transformed into other useful compounds through chemical or biological conversion (Deutschmann and Dekker 2012; Delgado Arcaño et al. 2020).

Xylitol is high-value-added pentose alcohol that can be converted from xylose. It is easily soluble in water and has a sweetness equivalent to sucrose, with fewer calories and a lower glycemic index. Xylitol presents constant pH in the range (1 and 11) and it has a high melting point of approximately 93 °C (Delgado Arcaño et al. 2020). This sugar has many applications in the food, drink, and health sectors (Deutschmann and Dekker 2012; Pulicharla et al. 2016).

In the food and drink industry, xylitol is used as a replacement for sucrose for caloric reduction. The most common use for this sugar worldwide is in sugar-free chewing gums. Xylitol is also used in the pharmaceutical industry mainly due to its proven anti-cariogenic properties, since it was demonstrated that substituting sucrose for xylitol for a 2-year period resulted in an 85% reduction in dental caries as well as a decrease of 50% in bacterial plaque growth (Lee et al. 2012a; De Albuquerque et al. 2014). Besides, xylitol is considered an appropriate sweetener for diabetics because the glucose produced from xylitol metabolism is released gradually from the liver, therefore its blood concentration does not suffer sudden changes (Molinary and Quinlan 2012).

Xylitol is produced at an industrial scale by catalytic hydrogenation of purified D-xylose solution under high temperature and pressure. However, microbial xylitol production is an alternative to the chemical process, as it occurs in milder conditions and the raw material can be derived from agro-industrial waste, operating at a low cost. Some yeasts and bacteria have the ability to ferment xylose. In a single-step production, xylose is reduced to xylitol in the presence of xylose reductase (EC 1.1.1.307) and can be either secreted or oxidized to xylulose by xylitol dehydrogenase (EC 1.1.1.B19). Xylitol production by microbial fermentation can be influenced by some factors, among them carbon and nitrogen source, aeration, temperature, and pH. Many kinds of researches to improve xylitol production via fermentation are focusing on continuous fermentation, using immobilized cells, since this method maintains high productivity for long periods and shows greater stability (Venkateswar Rao et al. 2016; Dasgupta et al. 2017).

Xylitol production has increased more than 40 times in the last four decades. In 1978, it was produced 6000 tons of xylitol and this number kept increasing over the years. In 2013 and 2017, xylitol production reached 161.5 and 190.9 thousand metric tons, valued at US$ 670 million and US$ 728.5 million, respectively. The forecast for 2022 is a production of 266.5 thousand metric tons, adding an amount of US$ 1 billion. The production cost of xylitol was estimated to be €59.2 per ton, using rye straw hemicellulose (Venkateswar Rao et al. 2016; Delgado Arcaño et al. 2020). These costs are mainly linked to the type of biomass used and transportation.

Another important product from xylose fermentation is bioethanol. The second-generation ethanol (E2G) originated from the lignocellulosic substrate has been studied for being an energy source and an alternative to the substitution of petroleum products. Mass balance studies suggest that the use of sugarcane leaves and bagasse for 2GE production may add alcohol yield to 1GE production, over 50% per ton of processed biomass (37.5% from cellulose and 21.3% from hemicellulose) (Stambuk et al. 2008).

The first step of producing bioethanol from lignocellulosic biomass is the pretreatment, a chemical-physical or biological process that in this case should aim to reduce the structural constraints to facilitate cellulose and hemicellulose transformation into monosaccharides (Melati et al. 2019). Co-fermentation of glucose (resulted from cellulose pretreatment/hydrolysis) and xylose (resulted from hemicellulose hydrolysis) is desirable (Gírio et al. 2010; Deutschmann and Dekker 2012).

Ideally, for lignocellulose ethanol production, microorganisms should display a broad substrate specificity, high ethanol yield, and productivity, besides having ethanol tolerance and tolerance to inhibitors present in hydrolysates. The common strain used for alcoholic fermentation from glucose (*Saccharomyces cerevisiae*—PE2) is not adequate for converting xylose or other pentoses into ethanol. Native yeast capable of fermenting xylose such as *Scheffersomyces stipitis and Scheffersomyces shehatae* has the ability to ferment both glucose and xylose. Although, ethanol production yield from xylose is usually lower than from glucose, mainly due to the less tolerance to the presence of inhibitors and ethanol concentration (Rodrussamee et al. 2018; Nweze et al. 2019).

2,3-Butanediol is a chemical with a broad spectrum of applications, mainly as a fuel additive but also with potential in the agriculture field as a pest control agent. The petrochemical route for its production could be replaced by a biological route. A variety of microorganisms can ferment monosaccharides (hexoses or pentoses) and produce BDO. BDO biosynthesis by bacteria occurs through a mixed acid-butanediol pathway, producing groups of an acid such as lactic acid, formic acid, acetic acid, and ethanol as co-products (Ji et al. 2011; Hazeena et al. 2020).

Bio-based isobutanol has received great attention due to its higher energy density, lower hygroscopicity, and high-octane value. By changing the metabolic pathway, a recombinant *S. cerevisiae* strain was able to produce isobutanol from xylose (Brat and Boles 2013). Terpenes are a group of natural products known as valuable sources of flavor, fragrance, and pharmaceuticals. Their extraction from natural resources is quite limited, usually low-yielding and inefficient. Metabolic engineering efforts are being made to improve its production. A positive effect of xylose utilization on terpene biosynthesis was demonstrated using an engineering *S. cerevisiae* strain (Kwak et al. 2017).

Lactic acid, a three-carbon carboxylic acid, can be obtained from hemicellulose materials fermentation. This compound is widely used in the food, chemical, and pharmaceutical industries. Currently, commercial production of lactic acid occurs by bacteria fermentation of glucose, and some of those strains are capable of utilizing hemicellulose-derived pentoses. Researches have shown that *Lactobacillus pentosus*, *Lactobacillus bifermentans*, *Rhizopus oryzae,* and a recombinant *S. cerevisiae* are able to convert xylose and glucose into lactic acid (Ji et al. 2012; Novy et al. 2018).

Pentose sugars (e.g. xylose from hemicellulose) is a notable substrate for obtaining several value-added products, favoring the use of lignocellulosic biomass in a biorefinery system, although there is often a need for the use of engineered microorganisms (Kwak et al. 2019).

## 11.3 Biomass Resources of Hemicellulose

Microorganisms and fermentation are very known in studies involving bioenergy, an example is the use of *S. cerevisiae* to produce ethanol by fermentation. Despite that, the studies and literature failed shortly when it is about hemicellulose fermentation and other microorganisms. The use of microorganisms to hemicelluloses sugar fermentation depends on the microorganism itself as well as the biomass source.

Biomass can be originated from agriculture, forestry, algae, and wastes, and be classified according to the chemical composition, origin, and end-use (Fig. 11.2) (Sánchez et al. 2019). One of the main suppliers of biomass with energy goals is the forest and wooded lands (Kummamuru 2017). Biomass from wood was progressively replaced by fossil fuel in the last century, however, the renewable potential of energy attracted attention. Approximately 2.4 billion people use wood to cook and heat as the main source of energy (FAO 2014). The forests cover almost 31% of the terrestrial land, yet this area has been decreasing 0.13% per year from 1990 to 2015, mainly in Africa and South America (Sánchez et al. 2019). Forests for energy use, such as those destined for the production of paper and cellulose, can be an interesting alternative for obtaining xylose.

Agricultural and agro-industrial by-products have been visible as important alternative energy potential. The agricultural energy crops can be separated into two categories: (1) crops for liquid biofuels, such as sucrose, starch, and oilseed and (2) crops for thermal applications or second-generation biofuels, like lignocellulosic materials (Brown and Le Feuvre 2017). This last group has received special attention for its use, mainly in regions where a given culture is predominant due to its edaphoclimatic characteristics and cultivable areas. A known by-product is the sugarcane bagasse, derived from sugarcane after a step in the broth extraction process. This by-product, particularly, can be used to generate electric energy from its burn (energy co-generation) or to generate second-generation ethanol.

In Brazil, sugarcane is the major crop for bioethanol, while maize is the primary crop in the USA and wheat and sugar beet for Europe (Long et al. 2015; Kluts et al. 2017). In this context, residual by-products of primary processes, such as the production of first-generation ethanol, to be used for the production of other value-added products within the biorefineries where the initial processing of biomass occurs (Forster-Carneiro et al. 2013).

The use of sugarcane bagasse and leaves (straw) stands out, as the country is the world's largest producer of sugarcane (*Saccharum spp*) (Alokika et al. 2021). The bagasse makes up about 1/3 of the biomass (Rocha et al. 2015). In the first-generation (1GE) ethanol production, sucrose is obtained by juice extraction from sugarcane stem. Sucrose, fructose, and glucose are efficiently converted into ethanol by the *S. cerevisiae* (fermentation process of Melle-Boinot). From this process, a large amount of residual by-products originates, especially bagasse and straw. It is estimated that for each ton of processed sugarcane in the sugar and alcohol industry, approximately 280 kg of residual biomass is generated (140 kg of bagasse and straw dry mass) (Dias et al. 2011), which by the quantity generated is important to develop alternatives methods for the use of these biomasses. Usually, the straw generated during the harvest is destined to cover the soil, while the bagasse is used in ovens for electricity and thermal energy production (Forster-Carneiro et al. 2013). However, it is estimated that about 1/3 of the bagasse and 1/4 of the straw are not yet used. The international economic scenario between 1974 and 1975 was decisive for the development of biofuel in the country, driven by high oil prices in international trade. At that time, the Brazilian government developed the National Alcohol Program (Pró-Álcool) from then on, the sugarcane was strategically directed to serve the biofuel market. According to estimates by CONAB (2019), the Brazilian production was 635 million tons, in a production area of 8.66 million hectares.

In the USA, corn is the main raw material for ethanol production as biofuel. Besides, corn is traditionally used in human and animal food due to its nutritional properties (Manochio et al. 2017). In the industrial process for ethanol production, the corn grain is crushed and undergoes different enzymatic hydrolysis stages (amylase, glucoamylase) for the release of glucose, which is fermented later. The process of saccharification (starch hydrolysis to obtain glucose through the action of glucoamylase) is performed concomitantly with fermentation (simultaneous saccharification and fermentation) (Devantier et al. 2005). During the corn harvest, by-products are generated, especially the corncob and the straw, from which

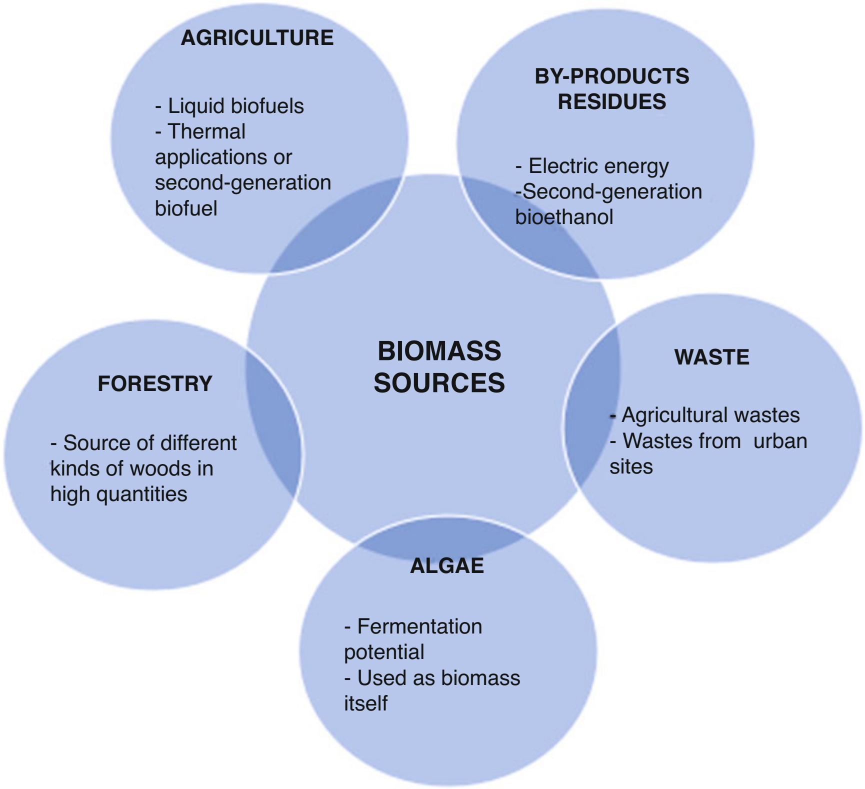

**Fig. 11.2** Visualization of different biomass sources

products of added value can be obtained through biotechnological processes similar to those used for sugarcane bagasse (Fig. 11.2).

Other major world markets for biofuels production include the ones that use sugar beet in the European Union; corn and wheat in China and Canada; and sugar cane in Thailand, India, and Argentina (Manochio et al. 2017). Besides the agro-industrial residues, there are residues from wood processing, which are applied to generate energy and by-products. There is also municipal solid waste as a potential energy source (Sánchez et al. 2019).

The last kind of biomass is algae, organisms from different rates including pro and eukaryotic organisms. There are more than 70 thousand species of algae, and this number increases every year (Barsanti and Gualtieri 2014). An important point to mention is the capacity of fermentation of some microalgae. From the algae, different kinds of products can be generated, for instance, as food for microorganisms in aquacultures (Behrens 2005).

## 11.4 Pretreatment Methods: Hemicellulose Hydrolysis and Degradation Products Formation

The hemicellulose hydrolysis involves a pretreatment (physical or chemical), where the depolymerization of primary structures in monomers occurs (Shimizu et al. 2020; Kumar and Sharma 2017). The hemicellulose can be solubilized with alkaline conditions (for example, using hydrogen peroxide) (Martins et al. 2021; Alves et al. 2020; Melati et al. 2021; Brienzo et al. 2016b), with combined biological and chemical treatment (Felipuci et al. 2021), and enzymatic or chemical hydrolyzed to produce oligomers or monosaccharides (Forsan et al. 2021; Freitas et al. 2019). However, among the usual methods are steam explosion and the use of concentrated and dilute acids in the context of biomass biorefinery.

The severity of the hydrolysis method applied to hemicellulose (temperature, hydrolysis time, pressure) directly implies the formation of degradation products, which are fermentation inhibiting compounds (Fig. 11.3). Mild conditions of temperature hydrolyze the hemicellulose easily due to its branched structure, generating a liquid rich in monomers of sugar that compose this polysaccharide (glucose, arabinose, and in higher concentration the xylose). Depending on the process condition, the hemicellulose can be partially hydrolyzed producing oligomers (Chiyanzy et al. 2015). Products of sugar degradation obtained from the depolymerization of hemicellulose represent an aggravating factor for efficient fermentation of xylose (Kumar and Sharma 2017; Perna et al. 2018).

Detoxification is an important technique that aims to minimize the effects of these contaminants on the fermentation. Several studies involve biological (Candido et al. 2020; Soares et al. 2016), chemical (Vallejos et al. 2016), and physical (Vallejos et al. 2016; Wang et al. 2018) processes for hydrolysate detoxification. Other conditions such as dissolved oxygen concentration and pH values established in the substrate during fermentation are essential to improve the conversion of sugar to bioproducts of interest (Taherzadeh et al. 2000).

The composition and concentration of inhibitors present in the lignocellulosic hydrolysate vary according to the biomass and the type of pretreatment applied. Inhibitors can be classified into four groups: (1) phenolic and aromatic compounds, resulting from lignin hydrolysis/degradation; (2) furan aldehydes, resulting from pentoses and hexoses degradation (dehydration reaction); (3) carboxylic acids, by-products from hemicellulose and furan derivatives degradation; and (4) soluble sugar, intermediate and final hydrolyzed products from lignocellulosic materials (Kim 2018). During the pretreatment that uses acid, the release of heavy metal ions (iron, chromium, nickel, and copper) can also occur, resulting from the corrosion of the equipment used in the acid hydrolysis (reactors), and it can inhibit the action of enzymes from the metabolic route of microorganisms (Mussato and Roberto 2004).

The presence of lignin in biomass restricts the enzymatic hydrolysis of carbohydrates, difficulting the access of cellulases to cellulose (Brienzo et al. 2015; Shimizu et al. 2020), causing an irreversible binding, besides contributing to the formation of pseudo-lignin in acid pretreatment (Schmatz et al. 2020a). The

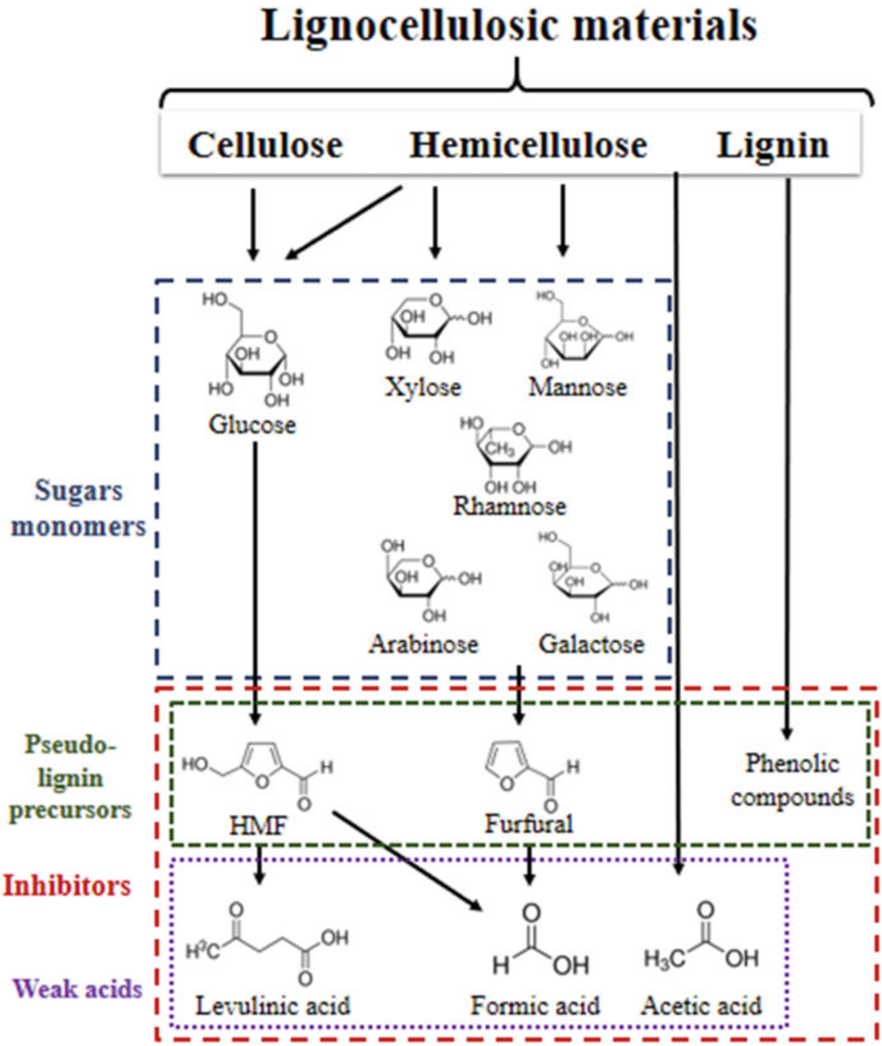

**Fig. 11.3** Brief scheme of the main inhibitory compounds formed in the hydrolysis of lignocellulosic biomass during acid and/or hydrothermal pretreatment

degradation of carbohydrates in acid pretreatment, mainly in high severity conditions (temperature, pressure, reaction time, and acid load) results in the formation of monosaccharides, which after dehydration reactions form furfural and 5-hydroxymethyl-furfural, from C5 and C6 sugar, respectively. These compounds have little effect on the inhibition of enzymatic hydrolysis but are harmful in the fermentation due to their toxicity to the fermenting microorganisms (Schmatz et al. 2020b). The degradation of furfural generates formic acid, however, the degradation of 5-hydroxymethyl-furfural generates levulinic acid and the partial decomposition of lignin generates phenolic compounds.

Different acids used in pretreatments dissociate the inter and intra-hydrogen bonds from cellulose, along with their glycosidic linkage, contributing to the degradation of sugar. Hexoses during hydrolysis are dehydrated to 5-(hydroxymethyl) furfural which contains a furan ring attached to an aldehyde group, and its toxic effect is widely known (Kumar et al. 2020).

The hemicellulose hydrolysis also releases acetic acid, which together with other weak liposoluble not-dissociated acids can diffuse through the plasma membrane of fermenting microorganisms, decreasing the cytosol pH, inhibiting the cell proliferation and viability. Although, there is a clear difference in toxicity between acetic, formic, and levulinic acids in the same concentrations, due to their differences in permeability of the plasma membrane and toxicity of the anionic form of acids (Palmqvist and Hahn-Hägerdal 2000).

Large quantities of compounds are released from lignin during the hydrolysis of lignocellulosic biomass (aromatic, polyaromatic, phenolic, and aldehydes), which have a considerable inhibitory effect on hydrolysate fermentation. These compounds cause rupture and loss of the integrity of the biological membrane, presenting as a consequence a decrease in the cell growth and assimilation of sugar by fermenting microorganisms. Even at low concentrations, these lignin derivatives present higher toxicity than furfural and 5-hydroxymethyl-furfural (Mussato and Roberto 2004).

Some types of microorganisms can metabolize low concentrations of furfural acid into furfuryl acid. This fact can be explained by the adaptation and synthesis of co-enzymes responsible for the reduction of furfural (Palmqvist and Hahn-Hägerdal 2000). Studies conducted with 64 different strains of different species of microorganisms inoculated in the hemicellulosic hydrolysate from the diluted acid pretreatment of sugarcane bagasse, revealed that only 5 are capable of growing at a concentration of 5 g $L^{-1}$ of acetic acid; 8 grew at a concentration of 0.4 g $L^{-1}$ of ferulic acid; only 1 at a concentration of 0.02 g $L^{-1}$ of 5-hydroxymethyl-furfural; and none at a concentration of 0.2 g $L^{-1}$ of syringaldehyde and 0.001 g $L^{-1}$ of furfural. However, some of these strains showed a decrease (remove/transform) in the combination of these toxic compounds present in hemicellulosic hydrolysate and can be interesting alternatives for use in detoxification (Soares et al. 2016).

The number of toxic compounds generated in the lignocellulosic hydrolysate may vary according to the biomass used and the operational conditions of the pretreatment. Variables in the fermentation process, such as cellular physiological conditions, pH, and dissolved oxygen concentration in the medium, as well as the combination of inhibitors, may also be associated, accentuating in several cases its toxic effect due to the synergistic action (Mussato and Roberto 2004).

### 11.4.1 Hemicellulose Hydrolysate Detoxification Methods

Among the strategies to minimize the formation of inhibitors before and after the pretreatment, it can be mentioned: the selection and/or engineering in the production of adequate raw materials that produce less unwanted compounds; chemical supplementation with alkalines, polymers or bovine albumin serum; biological detoxification through the use of microorganisms; evolutionary adaptation through the artificial selection of microorganism species with resistance to media with inhibitors; and use of genetic engineering to modify microorganisms and develop strains resistant to the inhibitors (Kim 2018).

Other strategies used in the detoxification of hydrolysates can be applied according to the specific need to eliminate a particular inhibitor. Among the existing physical methods, membrane filtration can separate phenolic acids from polysaccharides according to charge repulsion, hydrophobic adsorption, and molecular size exclusion of hydrolysate components. Ion exchange resins can be considered an economical technique because they present regeneration and reuse conditions and can be applied in the removal of salts, acids, and phenolic compounds. A simulated moving bed (SMB) consists of the separation of the compounds via chromatography and can be used in the separation of chemical compounds from petroleum, sugar, and pharmaceutical industries. The use of activated coal is a low-cost detoxification procedure that is used for various purifications (Kumar et al. 2020).

Among the chemical methods of detoxification, it can be mentioned the neutralization of the acid presented in the hydrolysate using caustic soda, lime, or another type of alkaline base before the purification by ion exclusion chromatography, adsorption, chromatography, or crystallization. As a result, lignin, proteins, and metal residues are precipitated. Liquid–liquid extraction (LLE) uses polar solvents to separate two miscible compounds, in which one dissolves especially one of them with properties such as those with low mutual solubility and low toxicity. The Sugaring-out extraction (SOE) technique is a phase separation method that consists of removing acetonitrile and sugar from the hydrolysate. The Sugaring-out process consists of the partitioning of compounds between two phases that can be formed by salts and polymers or hydrophilic solvents, hydrophobic solvents, and amphipathic chemicals (Kumar et al. 2020).

Biological detoxification processes are considered ecologically correct in which the application of specific microorganisms minimizes or eliminates toxic compounds from the lignocellulosic hydrolysate before enzymatic hydrolysis and can be used in conjunction with filter membranes (immobilization) (Kim 2018; Kumar et al. 2020).

The effectiveness of the detoxification method depends on the type of hydrolysate and microorganism used (different degrees of toxicity and different degrees of microorganism tolerance). If inhibitors of pretreatment are identified and inhibition mechanisms elucidated, the fermentation process can be improved by developing detoxification methods, selecting adapted microorganisms or improving fermentation strategies (Palmqvist and Hahn-Hägerdal 2000).

## 11.5 Microorganisms Used in Hemicellulose Sugar Fermentation and Xylose Metabolism

Monosaccharides obtained from hemicellulose can be used as substrates for bioproducts fermentation using different microorganisms. Hexoses (D-glucose, D-galactose, and mannose) and pentoses sugar (D-xylose, L-arabinose) can be converted into biochemicals such as organic acids, alcohols, xylitol, and 2,3 butanediol, among others (Chandel et al. 2018; Jiang et al. 2012; Canilha et al. 2013). In this review, the emphasis will be on the fermentation of xylose (C5 sugar), since this is the main monomer obtained from hemicellulose hydrolysis (McMillan 1993; Martins et al. 2018). Moreover, there is great potential in the development of fermentation processes aimed at using this sugar monomer.

Technologies for glucose fermentation are well established in terms of industrial yield with *S. cerevisiae* (Antunes et al. 2018; Passoth and Sandgren 2019; Kahar et al. 2011). On the other hand, technologies for hemicellulose sugar (xylose fermentation) are restricted to a few microorganisms and it is usually associated with low fermentation yield (Chandel et al. 2018). Therefore, the xylose fermentation represents an interesting route for the development and utilization of lignocellulose materials (Milanez et al. 2015; Gírio et al. 2010; Lamounier et al. 2020).

The ratio between consumed sugar and conversion into a product of biotechnological interest must be high in terms of industrial quantitative yield. This occurs, for example, with the fermentation of glucose to obtain first-generation ethanol (E1G). The yield of glucose fermentation for ethanol by *S. cerevisiae* reaches a practical yield of 92% (g ethanol/g sugar) (ferment C6 sugar to ethanol concerning theoretical yields). However, for the fermentation of xylose (hemicellulose materials), the best performing yield is 0.3–0.44 g $g^{-1}$ of the substrate, with yeasts of higher expression, such as *S. stipitis* (Stambuk et al. 2008). Besides, in glucose fermentation *S. cerevisiae* can withstand a wide range of inhibitors and high osmotic pressures (Fernandes and Murray 2010), in contrast, yeasts often used for xylose conversion have a low tolerance to osmotic pressure, to inhibitors, and also have a low cell growth rate (Canilha et al. 2013).

The metabolic capacity of some yeasts and bacteria to ferment xylose to value-added products has been described since 1960. There was an intensification of studies on the subject in the following decades, mainly due to industrial interest in the exploitation of this technology. Several research centers around the world sought to select and screen microorganisms with the ability to ferment xylose (McMillan 1993). In the last decade, a variety of microorganisms are described as being capable of fermenting pentose sugar in bioproducts of industrial interest, mainly for the ethanol, xylitol, and 2,3-butanediol production (Cheng et al. 2010; Ferreira et al. 2011; Martini et al. 2016; Xiao-Xiong et al. 2016; Hernández-Pérez et al. 2016; Guragain et al. 2017; Nakanishi et al. 2017; Martins et al. 2018; Rech et al. 2019). These strains fermented hydrolysates (xylose) into xylitol (0.2 to 0.8), ethanol (0.1 to 0.25), and 2,3-butanediol (0.45 to 0.5) in the range yields (g bioproduct/g sugar consumed).

One of the most studied bioproducts in terms of lignocellulosic biomass utilization is the second-generation ethanol (E2G). For ethanol production from pentose sugar, the optimum conditions yield was verified by Ferreira et al. (2011) using *Scheffersomyces stipitis* UFMG-IMH and obtaining productivity of 0.19 g $g^{-1}$ (incubation time of 96 h, pH 7). Martins et al. (2018) verified the ethanol production around 0.1 $g^{-1}$ by *Candida tropicalis* S4 from the xylose obtained from acid hydrolysate of hemicellulose. *Meyerozyma guilliermondii* in xylose fermentation produced 0.14 g of ethanol (g $g^{-1}$ sugar) in sugarcane bagasse hydrolysate with supplementation (Martini et al. 2016). Rech et al. (2019) using *Spathaspora hagerdaliae* (UFMG-CM-Y303) achieved alcoholic productivity in the order of 0.25 g $g^{-1}$.

The highest ethanol yields from hemicellulose materials (xylose fermentation) have been described with yeasts. Species such as *S. stipitis* and species of the genus *Candida* have been considered the most efficient (Hahn-Hägerdal et al. 1991).

Several biochemical reactions are required for the metabolization of xylose to occur under ideal conditions. One of the conditions that require more attention is oxygen supplementation. The xylose metabolization by yeast occurs through a redox process. Initially, D-xylose is reduced to xylitol with enzymatic action of D-xylose reductase, then xylitol is oxidized to D-xylulose by xylitol dehydrogenase, which through xylulose kinase reaction is transformed into D-xylulose-5-phosphate by the pentose phosphate pathway (Rastogi and Shrivastava 2017; Chandel et al. 2011). In bacteria, the conversion of D-xylose occurs directly to D-xylulose by the action of the xylose isomerase enzyme. Through enzymatic action (phosphopentose epimerase, transaldolase, and transketolase) D-xylulose-5-phosphate turns into glyceraldehyde-3-phosphate and fructose-6-phosphate leading to ethanol formation by Embden-Meyerhof Pathway (Chandel et al. 2011). In this biochemical machinery, oxygen concentration is a limiting factor in yeast ethanol production. Some yeasts achieve higher yields in terms of conversion from xylose into ethanol due to biochemical mechanisms that balance NADH and NADPH cofactors by the enzyme xylose reductase, under unbalanced conditions, there have limited $O_2$ supply. This regulation mechanism implies a lower conversion of xylose into xylitol (the accumulation of xylitol occurs due to the unbalance between NADH and NADPH) and consequently higher productivity of ethanol (the xylose reductase has a double dependency from both NADH and NADPH) (Granström and Leisola 2002; Granström et al. 2007).

Yeasts and bacteria are strictly dependent on parameters established in the fermentation process, such as the presence of chemical contaminants originated by sugar degradation, nutrient depletion, accumulation of final products, and physical and chemical conditions, such as pH and temperature (Ferreira et al. 2011; Taherzadeh et al. 2000). The pH regulation is essential for the maximum energy use of sugar to ethanol by the Embden–Meyerhof–Parnas Pathway. One of the main problems associated with the use of hydrolysates acids is related to the presence of organic acids, such as acetic acid, although some microorganisms can use it for their growth and maintenance. The excess of protons motivated by their acidic dissociation unbalances the intracellular pH with consequent energy waste and loss in the transport of nutrients (Van Zyl et al. 1991; Almeida et al. 2007). Consequently, energy waste affects the bioproducts' yield of industrial interest.

Bacteria and yeasts require specific conditions for most industrial applications. The low fermentation yield under industrial conditions is also due to low tolerance to high concentrations of a compound, such as ethanol (Meyrial et al. 1995), inhibitors formed during the pretreatment phase, and oxygen supplement conditions (Hahn-Hagerdal et al. 1994; Du Preez 1994).

The production of xylitol is obtained by reducing xylose to xylitol as the first step of xylose metabolism (Chandel et al. 2011) with the participation of NADPH-dependent xylose reductase (Granström et al. 2007; Hernández-Pérez et al. 2016). For xylitol production using *Meyerozyma guilliermondii* 0.19 g of xylitol (g $g^{-1}$ sugar) was obtained from sugarcane bagasse hydrolysate acid with supplementation (Martini et al. 2016). The maximum productivity of xylitol (0.56 g $g^{-1}$ xylitol/xylose) was observed under specific conditions (pH 6, temp. 28 °C, and 200 rpm) under substrate with 50 g $L^{-1}$ xylose. Alves et al. (1998) used *Candida guilliermondii* to ferment xylose (30 g $L^{-1}$) obtained a high concentration of xylitol (0.79 g $g^{-1}$) from supplemented hydrolyzed sugarcane bagasse acid. Hernández-Pérez et al. (2016) obtained a high concentration of xylitol (0.67 g $g^{-1}$) with *Candida guilliermondii* FTI 20037 using xylose as the main carbon source under the initial variable oxygen availability (sugarcane straw hemicellulosic hydrolyzate: xylose (50.60), glucose (9.75), arabinose (9.60)/g $L^{-1}$).

Butanediol is another important chemical product produced in the xylose fermentation. Li et al. (2014) using a thermophilic strain *Bacillus licheniformis* verified high productivity of 2.3 butanediol (0.45 g $g^{-1}$/80 h of the fermentation) with a total xylose concentration of 195 g $L^{-1}$ (fermentation was performed: 50 °C/pH 7.0/80 h with additional xylose when the concentration of xylose in the medium reached $<25$ g $L^{-1}$).

Other studies showed the production of 2,3-butanediol from the mixed-sugar medium. Guragain et al. (2017) obtained BD productivity values in the range of 0.30 g $g^{-1}$ in fermentation medium using the 2:1 ratio of glucose and xylose. However, these authors found that when the xylose and glucose were used in a single-sugar medium the productivity of 2,3-butanediol was higher: 0.45 g $g^{-1}$ xylose against and 0.42 g $g^{-1}$ glucose (Guragain et al. 2017). In their research, Cheng et al. (2010) found a maximum yield of 2.3-butanediol of 0.5 g $g^{-1}$ using mixed sugar with a predominance of xylose (120.1 g $L^{-1}$ xylose, 20.2 g $L^{-1}$ glucose, 12.8 g $L^{-1}$ arabinose, 0.8 g $L^{-1}$ cellobiose, 1.2 g $L^{-1}$ galactose, 0.7 g $L^{-1}$ mannose) from corncob hydrolysate acid using *Klebsiella oxytoca* ACCC 10370. In a synthetic medium containing only xylose (59.2 g $L^{-1}$), the BD productivity was 0.48 g $g^{-1}$.

Table 11.1 shows other studies for obtaining value-added products for different fermentation systems by sugar present in hemicellulose. The obtaining of added value products using hemicellulose materials (pentose fermentation) can occur via a fermentation process using naturally occurring microorganisms or through genetic improvement of non-fermentative lines of xylose.

**Table 11.1** Literature results for microorganisms to hemicellulose derivatives fermentation

| Microorganism | Carbon source and experimental conditions | $Y_{p/s}$ g g$^{-1}$ | Titer g L$^{-1}$ | Bioproduct | Reference |
|---|---|---|---|---|---|
| *Pichia stipitis NRRL Y-7124* | Xylose<br>Nutritional and oxygen requirements to maximize the xylose conversion to ethanol by *P. stipites* | – | [a]24.2 | Ethanol | Silva et al. (2012) |
| | | [b]0.33 | – | | |
| *Scheffersomyces stipitis NRRLY-7124* | Xylose (predominant medium)<br>Média of sequential batch cell recycle | – | 17 | Ethanol | Nakanishi et al. (2017) |
| *Spathaspora passalidarum NRRL Y-27907* | Glucose and xylose (predominant medium)<br>Average of sequential batch cell recycle | – | 21.8 | Ethanol | Nakanishi et al. (2017) |
| *Candida guilliermondii* | D-xylose (predominant medium)<br>The influence of the medium evaluated by growing the cells of *C. guilliermondii* either in the hydrolysate (containing mixed sugar and toxic compounds) or in semidefined medium (containing only xylose and lacking toxic compounds) | – | 6.5 | Ethanol | Rodrigues et al. (2006) |
| | | – | 1.5 | Glycerol | |
| | | 0.55 | 25 | Xylitol | |
| *Candida tropicalis* | Xylose (predominant medium)<br>The effect of inoculum concentration under different concentrations of xylose | 0.46 | 2.51 | Xylitol | Vallejos et al. (2016) |
| *Candida guilliermondii* | | – | 0.99 | | |
| *Clostridium saccharoperbutylacetonicum DSM 14923* | Xylose<br>Fermentative production from hemicellulose hydrolysates (xylose as the only carbon source) | 0.27 | 13.5 | Butanol | Chacón et al. (2020) |
| *Klebsiella pneumoniae CGMCC 1.9131* | Xylose<br>Production of 2,3-butanediol (2,3-BDO) with xylose obtained simultaneous saccharification and fermentation | 0.35–0.50 | | Butanediol | Zhao et al. (2011) |
| *Klebsiella oxytoca ACCC 10370* | Xylose<br>The effects of acetate in hydrolysate and pH on 2,3-butanediol production | 0.48 | 28.7 | Butanediol | Cheng et al. (2010) |
| *Klebsiella pneumoniae HR521 LDH (CGMCC 1.9131)* | Xylose<br>Effects of yeast extract, ethylenediaminetetraacetic acid disodium salt (Na2EDTA), and acetic acid on 2,3-BD production from xylose | 0.46 | 39.7 | Butanediol | Xiao-Xiong et al. (2016) |

$Y_{P/S}$ = ethanol yield (g ethanol/g sugar)

[a] Medium supplementation with nutrients

[b] Different oxygen transfer coefficient values

## 11.6 Improved Xylose-Fermenting Microorganisms by DNA Technology

The introduced pentose utilizing capability by microorganisms offers the possibility to convert lignocellulosic materials in bioproducts of industrial interest. Research has thus focused on developing new strategies in genetic engineering technology to create strains with more diverse substrate affinity and high inhibitors and ethanol concentration tolerance, increasing productivity (Harner et al. 2015).

Advanced techniques in synthetic biology and metabolic engineering enable the development of heterologous xylose-assimilating pathways for the production of value-added products (Zhang et al. 2011). The pathway introduced by genetic engineering for the production of a compound of interest considers the use of native pathways to provide key precursors, others are used due to the ease in handling biotechnological techniques, such as *E. coli*. Some microorganisms are a strategy to engineer xylose-fermenting: *E. coli, Z. mobilis, and S. cerevisiae* (Chandel et al. 2018). The most common strategy is cloning genes for the expression of xylose reductase and xylitol dehydrogenase in *S. cerevisiae* (Kim et al. 2013).

Some modified *S. cerevisiae* strains can produce xylan-degrading and xylose-fermenting enzymes and others can also ferment cellulose in one step without adding exogenous cellulolytic enzymes. *S. cerevisiae* is widely studied due to its widespread use in the industrial process (glucose fermentation), which favors issues related to safety and the fermentation process (Kim et al. 2014a). Extensive studies on metabolic pathways have resulted in genetically modified *S. cerevisiae* capable of fermenting pentoses sugar to value-added products (Cadete et al. 2016; Jo et al. 2017; Liu et al. 2018; Dijk et al. 2019). In a study using engineered *S. cerevisiae*, the authors show the productivity of 0.27 g $g^{-1}$ of BDO from xylose as a carbon source in a batch process (Kim et al. 2014b). Lee et al. (2012b) verified ethanol productivity in the order of 12 g $L^{-1}$ using xylose as a sole carbon source in microaerobic fermentation of recombinant *S. cerevisiae* (30 °C, 90 rpm; 80 h cultivation). Most of these approaches *S. stipitis* is used as a model microorganism due to its natural ability to ferment xylose.

In bacteria (pentose utilization), cloning involves heterologous expression of xylose isomerase (Brat et al. 2009). Thermophilic bacteria are also being engineered as an alternative approach. *E. coli* ability to secrete recombinant enzymes easily makes this microorganism a good candidate for industrial application. Another frequently used bacterium is *Z. mobilis*, a recombinant strain that showed an ability to produce ethanol of 0.44 g/$g^{-1}$ xylose (Zhang et al. 1995).

Despite the remarkable progress within recent years, the use of strains of genetically modified microorganisms is still controversial. Often, these microorganisms end up not being viable in industrial processes due to the lack of stability, which must be compensated with the use of complex culture media. However, the industrial process becomes unviable due to these costs. In addition, the use of pathogenic strains in industrial scale fermentation compromises the safety and industrialization of some bioproducts (Celińska and Grajek 2009). On the other hand, genetically modified strains capable of simultaneous saccharification and fermentation have the potential to reduce the costs of ethanol production in biorefineries (Deutschmann and Dekker 2012; Singla et al. 2012).

## 11.7 Conclusion

Hemicelluloses materials (crop and industrial by-products) are feedstock for alternative cheap and sustainable sugar supply and your bioconversion by fermentation routes in a wide variety of value-added products is an appropriate application for sustainable development. The bioenergy chain reduces the negative environmental impacts related to inappropriate disposal. Currently, the fermentative process (xylose fermentation) does not yet achieve feasible yields in terms of industrial production. Scientific efforts are being made to improve the pretreatment stages of lignocellulosic biomass, which may result in an improvement in the quality of the fractions obtained after pretreatment. Also, several types of research are focused on finding microorganisms capable of using efficiently the xylose. In addition to these advances, efforts are being made to produce yeasts and bacteria stronger through metabolic engineering for the use of xylose associated or not with glucose fermentation.

**Acknowledgments** The authors thank the São Paulo Research Foundation (FAPESP grant number 2017/22401-8; 2019/12997-6) for research support.

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# Production of Platform Chemicals and High Value Products from Hemicellulose

# 12

Elise M. Albuquerque and Marco A. Fraga

## Abstract

Transforming hemicellulose-derived carbohydrates into high value-added chemicals is still a challenge since upgrading these highly functionalized molecules involves several sequential reactions. Each reaction may require different operational conditions, like pressure, temperature and acidic or basic medium. For this reason, those reactions are usually performed in a multi-step process, with numerous reactors in series operating at different conditions. Alternatively, some one-pot single-step technologies have been pursued. This chapter presents some aspects on both technological routes. The direct transformation of hemicellulose and their derived pentoses, or hemicellulose-derived building blocks were considered. Only C5 molecules or lower carbon compounds are discussed. The hemicellulose-derived chemicals focused herein were separated in three major groups, namely furans (furfural and furfuryl alcohol), polyols (xylitol, ethylene glycol and propylene glycol) and organic acids (levulinic and lactic acids).

## Keywords

Pentoses · Furfural · Xylitol · Ethylene glycol · Levulinic acid · Lactic acid

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M. Brienzo (ed.), *Hemicellulose Biorefinery: A Sustainable Solution for Value Addition to Bio-Based Products and Bioenergy*, Clean Energy Production Technologies, https://doi.org/10.1007/978-981-16-3682-0_12

## 12.1 Introduction

Identifying drop-in chemicals, i.e. chemicals that can be obtained from biomass but are identical to those already produced by the chemical and petrochemical industries and used in other industrial sectors, is usually the first approach in a biorefinery context. This is a safe approach indeed as there is already an established product market with a known demand to be supplied. On the other hand, the wide variety of other possible chemical structures derived from biomass demands the development of technologies to transform these new chemical structures into marketplace products and the organization of new markets for them. No matter the approach, biomass conversion technologies still need to be developed and that is the major technological hurdle in the biorefinery rise.

In the pursuit of identifying these compounds, by the beginning of the twenty-first century, the US Department of Energy (DOE) acknowledged the strategic role played by some platform chemicals that could be produced from carbohydrate feedstocks (Werpy and Petersen 2004). That report highlighted bio-derived chemicals, which can be organized in two major chemical classes: carboxylic acids and polyols. They were selected based mostly on their chemical's properties, market data and industrial viability. A few years later, that report was revisited and some compounds were excluded while some others were added to this potential group of bio-based chemicals (Bozell and Petersen 2010). The proposed list was then composed by four chemical groups: carboxylic acids, polyols, furans and hydrocarbons. Substantial advances in the conversion of carbohydrates to those chemicals have been achieved from that first DOE report mainly due to extensive research activity worldwide.

Converting renewable carbon from carbohydrates is indeed the key challenge for the biorefining industry. It is particularly true when the demanded technologies are compared to the processes relying on classical non-renewable sources, such as oil, coal and natural gas. Indeed, carbohydrates are highly functionalized molecules, holding many oxygen functional groups and thus their upgrading may entail multiple sequential reactions. Therefore, carbohydrate conversion technologies are quite demanding from both chemical transformations and chemical engineering process design.

Cascade reactions are often involved in the conversion of carbohydrates and they usually comprise a combination of isomerization, dehydration, hydrolysis or hydrogenation/hydrogenolysis reactions. Each of them may require different operation conditions, mainly pressure and temperature, or need a specific reaction medium as those transformations may proceed in acidic or basic conditions under reducing or oxidizing atmospheres. Consequently, multi-step processes performed in several chemical reactors, which may operate in series, are a possible approach. In such a process design, the specific conditions for every single reaction step can be tuned to lead to high product final yields. Batch reactors are largely used in research activity as they are suitable for small scale and they are also more readily available in research laboratories. Nonetheless, they are very limited and less attractive for larger industrial processing volumes, which is the case in carbohydrate biorefineries as large volumes of low-concentration streams have to be upgraded. Continuous reactors, on the other hand, are more advantageous both on the development of lab-scale catalysts and on the evaluation of any potential industrial application (Yue 2018; Tanimu et al. 2017; Hartman et al. 2011). Moreover, continuous reactors are more suitable to perform reaction kinetics, transport phenomena and deactivation studies (Sievers et al. 2016). Research activity, however, is still scarcely carried out in such chemical reactors. Transitioning from batch to continuous processes is highly necessary to the growth of carbohydrates biorefineries.

One-pot process, when multi-step reactions are promoted in just one single reactor, is an alternative for those multiple reactors process assembly both in batch and continuous mode. The establishment of a single-step reaction is also highly pursued. Either process intensification strategy can allow the development of more compact, efficient and more competitive new processes, addressing important aspects related to energy consumption or waste generation while attaining high productivity (Sitter et al. 2019).

In that trail, the role played by catalysts should be highlighted as they are central in the chemical transformation technologies. All those above-mentioned carbohydrate conversion possibilities are promoted by a catalyst, may it be homogeneous, heterogeneous or a biocatalyst. Homogeneous catalysts can be highly active but they are more difficult to be separated from the reaction medium and recycled. Once it is done, they usually require special attention on disposal to mitigate the whole process environmental impact. The use of heterogenous catalysts, on the other hand, brings the possibility to overcome such problems. As they are solids, they are easily recovered from the reaction medium and they can be reused in multiple reaction cycles. In many cases they can also be regenerated once their activity starts decaying. It should also be mentioned that they can address the corrosiveness issues commonly involved in homogenous catalysed processes. It is indeed a relevant technological matter due to the aggressive nature of homogeneous catalysts, which are usually mineral acids and hydroxides in industrial applications. Lastly, biocatalysts are reckoned for their high selectivity, which is very important for downstream processing. However, microorganism-based bioconversion processes can be complex as they necessitate very specific and controlled conditions, and nutrients for their cultivation and growth. Furthermore, they are also sensitive to the minor presence of inhibitory compounds in the reaction medium, which is quite challenging when converting carbohydrates, imposing prior detoxification steps (Rafiqul and Sakinah 2013). In this chapter, special focus is given to the production of value products obtained from heterogeneous catalysed reactions. Therefore, the conversion of hemicellulose sugars through homogeneous or biochemical pathways is not within the scope of this work.

Similar to other carbohydrate fractions, saccharides released from hemicellulose are low vapour pressure compounds extremely soluble in water. Indeed, water is always present since either those sugars are released in aqueous solution upon biomass fractionation or water is produced along their upgrading. Therefore, hemicellulose biorefinery technologies are expected to be based on chemical process in aqueous solution. On one hand, it is very attractive and desired as water is a green, friendly solvent that brings no concern on handling, toxicity and environmental impact. On the other hand, the presence of water brings some challenges as regarding the stability of highly functionalized compounds. It is indeed known that some sugar-derived chemicals tend to polymerize in high concentration aqueous solution or even in diluted solution when in the presence of acid solids (van Zandvoort et al. 2013). The formation of those high weight compounds along with solid by-products or humins occurs via complex condensation reactions whose mechanism have been studied more recently (Xu et al. 2020a). Such understanding is crucial to suppress humins formation upon carbohydrates upgrading or to identify new technologies to valorise them whether their formation is inevitable in a specific and yet productive process.

Aqueous-phase processing of hemicellulose sugars also brings some concern when relying on heterogeneous catalysts. Solid catalysts must be hydrothermally stable at moderate temperature and high amount of water. That is to say that the catalyst cannot undergo irreversible structural changes or lose its textural properties since it can lead to different surface properties undermining the catalyst performance in sequential reaction cycles. Additionally, the catalyst needs to be chemically stable under basic or acid conditions and be resistant to leaching that could cause deactivation and the contamination of the final product. Lastly, the interaction of water molecules with the solid surface should be carefully considered, particularly when acid-catalysed reactions are involved. The formation of water-acid sites adducts may lessen the catalyst surface acidity turning it a poorly active catalyst for aqueous-phase processing of hemicellulose sugars.

This chapter focuses on presenting some aspects regarding the synthesis of valued compounds catalytically produced from hemicellulose sugars. Processes relying either on the straight transformation of hemicelluloses or their derived pentoses or on the conversion of a hemicellulose-derived building block were considered in this selection. As a consequence, only compounds with a C5 or lower carbon backbone chains are discussed with particular attention to the aqueous-phase chemocatalytic processes. The hemicellulose-derived green chemicals are herein presented in three major groups out of those appointed by the original DOE report on strategic biomass-derived molecules, namely furans (furfural and furfuryl alcohol), polyols (xylitol, ethylene glycol and propylene glycol) and organic acids (levulinic and lactic acids), as summarized in Fig. 12.1. In all cases, their use in different bioeconomy sectors was highlighted, which covers mostly polymers, fuel additives, food and solvents. Nonetheless, it is important to outline that extensive reviews on those processes were not intended herein since many excellent review papers have been published, collecting recent advances. They will be referenced accordingly to support further reading on the subject. This chapter, therefore, aims at organizing the main strategies presented so far to produce the selected high value green chemicals critically pointing out their advantages and drawbacks within the challenge of establishing a hemicellulose biorefinery.

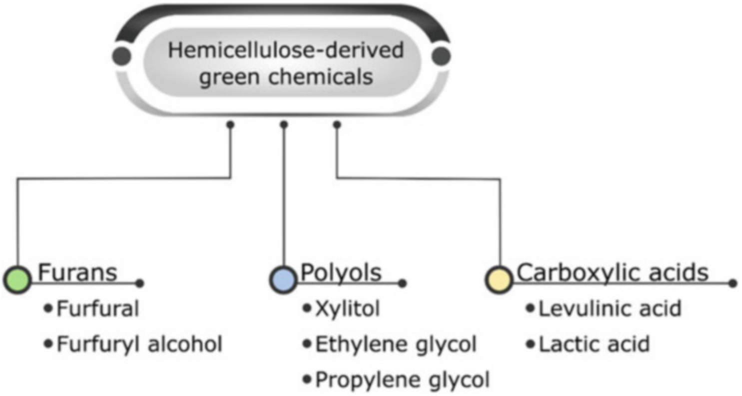

**Fig. 12.1** Hemicellulose-derived chemicals addressed in this chapter

## 12.2 Furans

Furans are probably the main chemicals industrially obtained from hemicelluloses. This class of compounds would have no obvious petrochemical alternative and the technologies for producing some of them are already long known and commercially used. Furfural is the most appealing of them all due to its versatility as a chemical platform (Yan et al. 2014). Furfuryl alcohol also stands out as around 60–70% of furfural output is directed to its production through hydrogenation, which makes furfuryl alcohol the main industrial green chemical produced from hemicelluloses. Therefore, the catalytic transformation of hemicelluloses or xylose into these two furans will be taken herein to outline the most relevant technical issues related to the production of high value furan chemicals.

### 12.2.1 Furfural

Furfural has long been produced from biomass and the Quaker Oats process is the oldest way of manufacturing it, dating back from the early 1920s (Peters 1936). Strong mineral acids, mainly $H_2SO_4$, are used as homogeneous catalysts, which demands restrictive attention because of corrosiveness and an effective downstream treatment due to the acid nature of the process waste. These are only some of the substantial drawbacks of this process that are largely acknowledged and have been already widely discussed over the years.

This scenario has motivated extensive studies towards the development of new processes based on acid solids, the exploitation of more suitable process conditions (pressure and temperature) and the use of extracting techniques aiming at improving furfural yield (Serrano-Ruiz et al. 2011). As a consequence, catalysts surface properties, reaction mechanism, kinetics and deactivation have all been investigated in detail. Indeed, several consistent reviews have been published over the last years covering the various routes for furfural production (Lange et al. 2012), its direct synthesis from hemicellulose in lignocellulosic biomass (Luo et al. 2019), challenges in using ionic liquids (Peleteiro et al. 2016), catalytic mechanisms in homogeneous systems (Zhao et al. 2021) and the development of different types of heterogeneous catalysts (Delbecq et al. 2018; Agirrezabal-Telleria and Arias 2014). Hence, only the main aspects related to the start of the art will be briefly outlined herein.

It is now known that the rate of pentoses dehydration is dependent on their molecular structure. Xylulose, which is the ketopentose isomer of xylose, is more readily dehydrated to furfural over Brönsted acid sites than the primary hemicellulose-derived aldopentose form (Choudhary et al. 2012). The co-presence of Lewis acid sites markedly improves the catalyst performance as they promote xylose isomerization to xylulose. Therefore, mechanistically, xylose is directly dehydrated over Brönsted acid catalysts whereas a cascade pathway takes place when Lewis-Brönsted acid sites are combined on the catalyst surface. The wide variety of heterogeneous catalysts already investigated, which includes heteropolyacids, ion-exchange resins, zeolites, mesoporous molecular sieves, clays, 3D and exfoliated 2D transition metal oxides, phosphates and carbon materials, allowed the conclusion that selectivity to furfural is dependent on the nature of the acid site and it can be improved by tuning the balance between Brönsted and Lewis acid centres; an increase in such ratio leads to an increase in furfural selectivity. This trend has also been verified for homogeneous acid catalysts (Weingarten et al. 2011). Some authors argue that, besides catalysing xylose isomerization, Lewis acid sites promote undesired side reaction yielding humins (You et al. 2014; Weingarten et al. 2011). Furfural degradation and reactions between xylose and furfural are the leading routes involved in humins formation and decrease in furfural yields in aqueous-phase processing (Weingarten et al. 2010).

Performing xylose dehydration in non-aqueous phase has been investigated as a way to avoid carbon loss through humins formation. Indeed, a wide range of organic solvents with different properties and functional groups has been evaluated, which includes alcohols, ketones, furans, ethers, esters, hydrocarbons and aromatics. Monoalcohols can stabilize reactive intermediates increasing the selectivity to furfural (Hu et al. 2012). However, some alcohols can take the reaction further and yield alkyl levulinates through a sequence of transfer hydrogenation/esterification reactions (Hu et al. 2014). Dimethyl sulfoxide (DMSO) can also lead to high furfural yields by providing a shielding effect (Karinen et al. 2011). Furfural is rapidly produced in diethyl ether, hexadecane, toluene and guaiacol, but its degradation is similarly fast. Ketones and furans, except tetrahydrofuran (THF), react with both xylose and furfural and thus are not recommended solvents (Hu et al. 2014).

Liquid–liquid extraction with organic solvents has also been disclosed as an effective strategy to avoid humins formation and enhance furfural yields. Toluene (Román-Leshkov et al. 2007), dichloromethane (Deng et al. 2016), dioxane (Chheda and Dumesic 2007), dimethyl formamide (DMF) (Li et al. 2014), THF (Xu et al. 2018), methyl isobutyl ketone (MIBK) (Yemis and Mazza 2012), cyclopentyl methyl ether (Molina et al. 2012), 1-butanol (Zhang et al. 2012), 2-pentanone

(An et al. 2019) and DMSO (Wang et al. 2014) are amongst the organic solvents used in this approach, being toluene by far the most explored one. In water-toluene biphasic system, furfural is extracted into the organic phase hindering its condensation and degradation reactions that usually occurs in water (Li et al. 2014; Gürbüz et al. 2012).

Despite all these detailed studies presented so far in the literature, choosing a suitable organic solvent for producing furfural has to consider the whole process sustainability. Green solvents with high volatility that can enable an easy separation from furfural should be taken.

Finally, it should be pointed out that the catalyst porous network also deserves attention when developing a catalytic technology. Strong furfural adsorption on microporous materials has been shown to favour furfural decomposition or polymerization reactions leading to humins (Weingarten et al. 2011). Indeed, despite some good results already reported over zeolites (Delbecq et al. 2018), catalyst pore confinement brings about adverse effects on the process selectivity (Weingarten et al. 2011).

### 12.2.2 Furfuryl Alcohol

Production of furfuryl alcohol is currently performed through hydrogenation of furfural. As a consequence, it is a two-step process at which furfural is firstly produced from hemicellulose and then reduced to furfuryl alcohol (Wang et al. 2019). As an alternative, a single-step intensified cascade process using xylose as feedstock has also been investigated over recent years (Coelho et al. 2020; Albuquerque et al. 2020; Perez et al. 2019, 2017; Canhaci et al. 2017; Perez and Fraga 2014). In this approach, xylose dehydration to furfural and further reduction to furfuryl alcohol are sequentially promoted in the same reactor over multifunctional catalysts.

The efforts to develop catalytic technologies to produce furfuryl alcohol are driven by its importance in different chemical industry segments. It is used to produce poly(furfuryl alcohol), which is a polymer with remarkable chemical stability to several solvents (Antunes et al. 2012), it is also a central fine chemical intermediate for producing vitamin C and lysine (Wettstein et al. 2012), it can also be used in the manufacturing of lubricant, plasticizers and dispersing agent (Millán and Sixta 2020), and to obtain levulinic acid, another quite strategic hemicellulose-derived platform chemical (Bozell and Petersen 2010), and 2-methylfuran, appointed as a potential biofuel or fuel bioadditive (Yan and Chen 2013). Due to this industrial relevance, some systematic reviews have deal with furfuryl alcohol production both from furfural selective hydrogenation (Wang et al. 2019; Yan et al. 2014) and one-step xylose conversion (Millán and Sixta 2020). Broader scope reviews have also dealt with such transformations (Millán et al. 2019; Lange et al. 2012).

Tuning product selectivity needs careful attention since a wide variety of chemicals can be produced in furfural hydrogenation process as depicted in

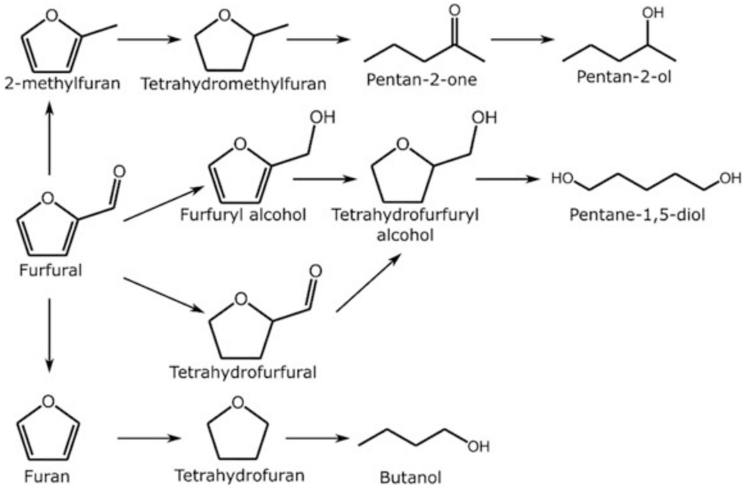

**Fig. 12.2** Furfural possible hydrogenation products

Fig. 12.2. Furfuryl alcohol is obtained by hydrogenating the furfural carbonyl group while keeping the C=C bonds in the furan ring.

#### 12.2.2.1 Two-Step Technology

In the two-step process, furfuryl alcohol is obtained from furfural hydrogenation, which is promoted over copper chromite catalysts at $H_2$ pressure around 30 bar and temperature within 130–200 °C. Despite the high yields achieved over CuCr system, the high toxicity of Cr, the changes in Cu oxidation state upon reaction and the catalyst strong deactivation have been motivating the search for some alternative processes. The first expected approach is to get rid of Cr in the Cu-based catalyst formulation, relieving the potential hazard to health and environment embodied by it. Keeping Cu, on the other hand, can be advantageous as it is an effective hydrogenation catalyst available at low price.

Different supports have been evaluated to examine the impact of their acid-base properties on Cu deactivation and the preservation of active Cu species along reaction. Introducing basic sites on the catalyst surface seems to lead to more suitable catalysts (Wang et al. 2017a, b) and remarkable furfuryl alcohol selectivity of 96% was accomplished over some systems (Hu et al. 2016). Indeed, much lower yields have been reported with more inert $SiO_2$ (2%) (Dong et al. 2015) and SBA-15 (52%) (Vargas-Hernández et al. 2014), amphoteric ZnO (70%) (Jiménez-Gómez et al. 2016) or redox $CeO_2$ (71%) (Jiménez-Gómez et al. 2017) supports. Acidic materials such as HZSM-5 and $Al_2O_3$ have been reported to provide higher selectivity towards 2-methylfuran and oligomers (Wang et al. 2017a) due to a claimed synergistic effect between metal and acid sites (Dong et al. 2015).

Another key point driving product selectivity is the distribution of Cu species on the catalyst surface. The balance between $Cu^+$ and $Cu^0$ has shown to be needed for selective furfural reduction (Gong et al. 2018a, b; Zhang et al. 2014). Such balance can be tuned by choosing a suitable support, as those already pointed out hereinbefore, but it can also be adjusted by a second metal in a bimetallic catalyst. Co, Ni and Fe are commonly used in this approach as they are low-price high active metals as well. Some studies showed that high furfuryl alcohol yields are achievable over bimetallic Cu catalysts even when supported on less favourable oxides. Indeed, contrastingly higher yields were accomplished when Cu-Co bimetallic phases were supported on both $SiO_2$ (53%) (Srivastava et al. 2018) and SBA-15 (80%) (Srivastava et al. 2015) with a remarkable performance on C (90%) (Wang et al. 2017b). On the other hand, acidic supports still led to poor results as Cu-Co/$Al_2O_3$ and Cu-Co/HZSM-5 reached furfuryl alcohol yields of only 11% and 28%, respectively (Srivastava et al. 2018). Similar behaviour was reported by using Cu-Fe systems (Manikandan et al. 2016) while Cu-Ni catalysts are definitely more selective towards either 2-methylfuran or tetrahydrofurfuryl alcohol (THFA) according to the operation conditions (Wu et al. 2017; Liu et al. 2016a; Yang et al. 2016a). These trends are in line with the performance of monometallic Ni and Co supported catalysts. Reaction data reported so far consistently showed that Ni promotes deeper hydrogenation and the product distribution is sensitive to reaction conditions (Wang et al. 2019) whereas Co catalysts can provide high furfuryl alcohol yields (95–98%) (Jiang et al. 2018; Gong et al. 2018a; Lee et al. 2015).

Noble metal-based catalysts are also an alternative for the production of furfuryl alcohol from furfural hydrogenation preceded by xylose dehydration step. Stability in aqueous-phase is not the main issue in this case but maximizing yields is a must due to noble metals higher cost. Controlling selectivity is challenging as they are usually very active metals for hydrogenation reactions potentially leading to more reduced products.

While THFA and 2-methylfuran are, respectively, more easily obtained over Pd and Ru catalysts, higher furfuryl alcohol yields are achieved over Pt-based systems. Synthesizing furfuryl alcohol at yields above 85% was only possible on Ru supported catalysts by running the reaction at low temperatures (20 °C), as reported over the last few years by Ramirez-Barria et al. (2018), Yang et al. (2016b) and Yuan et al. (2015). Using a bimetallic Ru-Sn phase is also a possibility as demonstrated by Musci et al. (2017). As regarding Pd catalysts, controlling reaction temperature (90–150 °C) (Ouyang et al. 2018; Garcia-Olmo et al. 2016) and the metal nanoparticle size (~8 nm) (Bhogeswararao and Srinivas 2015) are leading points, rendering yields around 70%. Better performance was only noticed over bimetallic Pd-Cu catalysts, over which 98% was obtained (Fulajtárova et al. 2015).

Contrastingly, product selectivity was not affected by the average size of metal nanoparticles in supported Pt catalysts as meticulously examined in the recent review by Wang et al. (2019). Yields above 90% are reported for simple Pt systems at temperatures in the range 80–100 °C. This behaviour is associated with the higher hydrogenation activity of Pt for carbonyl groups instead of the reduction of C=C bonds in the furan ring. Despite such good performance, bimetallic Pt catalysts have also been aimed due to the aforementioned high cost and metal availability. Different non-noble metals has also been investigated and high yields (87–100%) were preserved by using Co (Dohade and Dhepe 2017), Cu (Huang et al. 2016), Fe (Liu et al. 2018a), Re (Chen et al. 2015) and Sn (Maligal-Ganesh et al. 2016).

Mechanistic insights on furfural hydrogenation considering the nature of the metal sites in heterogeneous catalysts can be found in a recent review by Millán and Sixta (2020).

#### 12.2.2.2 Single-Step One-Pot Process

Despite all the advances both in xylose dehydration over heterogeneous catalysts and in chemoselective hydrogenation of furfural towards furfuryl alcohol in the search for a greener environmentally friendly technology, it is still a two-stage process that must be assembled in a multiple reactor process design. The development of an integrated technology at which the reaction can proceed in just one chemical reactor and preferably over one multifunctional heterogeneous catalyst is highly desirable.

The feasibility of a one-pot process was first unveiled over a dual acid-metal catalytic system constituted by a solid acid and a noble metal catalyst using a batch reactor (Perez and Fraga 2014), which later evolved to a single multifunctional catalyst (Perez et al. 2017). Perez and Fraga (2014) reported a furfuryl alcohol selectivity of 55% by using a mixture of sulphated zirconia and Pt/$SiO_2$, whose performance was largely influenced by the water/2-propanol ratio used as solvent, and the reaction temperature. The authors also stressed that the reaction dynamics plays a major role in determining product distribution. Indeed, the kinetics of each cascade reaction step (xylose dehydration and furfural hydrogenation) is crucial when acid and metal sites are placed on different solid surfaces. Nonetheless, arranging both the sulphate acidic groups and $Pt^0$ nanoparticles onto a single catalyst surface disclosed that the balance between those sorts of sites requires special attention (Perez et al. 2017). The occurrence of isolated metal centres allows the production of xylitol as a consequence of the direct hydrogenation of xylose. Conversely, higher selectivity towards furfural is reached at higher concentration of acidic surface sites. Vicinal acid-metal pair sites are claimed to optimize the direct production of furfuryl alcohol from xylose (Perez et al. 2017). A remarkable selectivity of ~90% was reported by Canhaci et al. (2017) over a single multifunctional hybrid Pt catalyst. These authors supported metal nanoparticles on an organic-inorganic hybrid mesoporous SBA-15 on which sulfonic groups were grafted to provide the required acidic sites. The presence of $-SO_3H$ moieties hindered the direct hydrogenation of xylose to xylitol, allowing the cascade conversion to furfuryl alcohol at high selectivity (83–87%) at 130 °C. The mesostructure of the proposed hybrid catalyst was well preserved during xylose aqueous-phase processing but a poor leaching resistance was verified as sulfonic groups were lost under the reaction conditions. Such vulnerability was also reported when sulphate groups were used to impinge acidic properties to the solid catalyst (Perez et al. 2017). Both studies (Canhaci et al. 2017; Perez et al. 2017) credited the catalyst deactivation to the hydrolysis of the sulphate or sulfonic acidic surface groups.

Other research groups focused on using non-noble metal catalysts and transitioning from batch to flow reactors. Cui et al. (2016) combined a Hβ zeolite as acid solid and $Cu/ZnO/Al_2O_3$ as metal catalyst in a double bed flow reactor for direct conversion of xylose in water/γ-butyrolactone. Furfuryl alcohol yield could be driven by the relative amount of each catalyst and it was optimized to reach 87% of furfuryl alcohol at 150 °C. The acid catalyst was seen to deactivate first but it could be reactivated leading to a full activity recovery. No Cu leaching was reported in this continuous process design.

Cu was also investigated as a non-noble metal phase on a sulfonated SBA-15 support (Deng et al. 2020) in a catalyst architecture similar to that firstly presented by Fraga's research group (Canhaci et al. 2017). In this study, Deng et al. (2020) reported a 63% furfuryl alcohol yield, which was formed alongside xylitol, furfural and 2-methylfuran at 140 °C in a water/*n*-butanol biphasic solvent mixture. The production of the sugar alcohol was attributed to high $H_2$ pressures whereas higher temperatures were credited with leading the reaction to 2-methylfuran. No information on Cu or sulfonic groups stability was provided though.

These technology approaches rely on xylose dehydration and furfural metal-catalysed hydrogenation cascade reactions. Even though high furfuryl alcohol yields were already reported and some significant progress has been made towards a greener technology, these processes require expensive molecular $H_2$ and are run under high pressures. These conditions can potentially increase the total cost and hinder industrial application. Alternatively, hydrogenation step can be performed via Meerwein–Ponndorf–Verley (MPV) mechanism at which a sacrificing alcohol donates a hydride to the aldehyde group in the liquid reaction medium. Using alcohol as a hydrogen donor can also benefit the reaction carbon balance as intermolecular interactions established between xylose or furfuryl alcohol with the sacrificing alcohol molecules can prevent polymerization side reactions by inhibiting the formation of reactive carbocation species (Kim et al. 2013).

Zeolites with different topologies, namely MFI, FAU and BEA, have thus been investigated in dehydration–transfer hydrogenation reactions of xylose to furfuryl alcohol (Paulino et al. 2017). The presence on zeolite surface of both Brönsted acid sites, needed in the first dehydration step (Choudhary et al. 2012), and Lewis acid centres, demanded for the MPV hydrogenation (Corma et al. 2002), makes them promising catalysts. Beta zeolite was found to be a more suitable catalyst, leading to yields of furfuryl alcohol of around 80%. Authors claimed that the configuration of tetrahedral framework Al-Lewis sites dictated by Al-O-Si bonds in beta zeolite and its large pore three-dimensional structure play a central role in the catalyst performance (Paulino et al. 2017). Much poorer performance was indeed undeniably observed on USY, rendering only 35% yield.

The influence of the nature, strength, amount and distribution of acid sites on beta zeolite on aqueous-phase conversion of xylose to furfuryl alcohol was also recently studied (Coelho et al. 2020). It is now known that product distribution is determined by the balance between water-tolerant Lewis and Brönsted acid sites, being furfuryl alcohol selectivity higher as this ratio is closer to 1. Coelho et al. (2020) also showed that the BEA framework is structurally and chemically resistant upon aqueous-phase reaction at mild conditions (130 °C) but Al leaching occurs with the increase in temperature even though no structure collapse was detected. Also important is beta zeolite regeneration and reusability as carbonaceous deposits could be burned off recovering catalyst activity and rendering the same product pattern (Coelho et al. 2020).

USY and BEA zeolites modified with Zr have also been evaluated for the direct conversion of xylose. However, incorporating Zr in the framework of those zeolites led the reaction to go further producing levulinic acid or γ-valerolactone (López-Aguado et al. 2018; Melero et al. 2017; Hernández et al. 2016). The strategy to embed Zr is also critical as the cascade reaction can be halted if the surface Brönsted acid sites are vanished upon synthesis (Albuquerque et al. 2020).

Lastly, Al-modified mesoporous SBA-15 catalysts were also recently investigated and they were shown to be highly selective to furfuryl alcohol (90–95%). Similar to the zeolite's behaviour, selectivity was reliant on Al amount into the molecular sieve framework and the mesostructure was also stable under the aqueous-phase processing conditions (Perez et al. 2019). The good performance of mesoporous molecular sieves brings the possibility of catalytic upgrading hemicellulose hydrolysates coming from different processes, including those at which high amounts of larger xylooligosaccharides are present. This catalyst architecture expands the opportunities to value hemicellulose fraction towards furfuryl alcohol and other bioproducts in a biorefinery.

## 12.3 Polyols

Hydrolytic hydrogenation of hemicellulose and hydrogenation/hydrogenolysis of pentoses unlocked from hemicellulose are the processes involved in the production of polyols. Hydrolytic hydrogenation is a one-step and one-pot route that involves the hydrolysis of hemicelluloses into sugars, followed by their hydrogenation to polyols. Hydrogenation of pentoses, on the other hand, takes a hemicellulose hydrolysate as feedstock. Therefore, in this case, it is preceded by a hydrolysis step intentionally carried out to provide hemicellulose sugars to obtain polyols or it uses a waste hydrolysate, which is commonly a sidestream from another biomass-based process. In this configuration, the main biomass-based technology is devoted to upgrading cellulose or lignin fractions as it is usual in biofuel production processes; producing polyols or any other high value chemicals is thus an approach to a cost-competitive circular bioeconomy technology. Figure 12.3 schematically illustrates these pathways towards hemicellulose-based polyols.

Both reaction routes are carried out in the presence of hydrogen and require a metal catalyst. However, transfer hydrogenation reaction has also been reported to produce sugar alcohols from xylans with xylitol yield above 80% (Yi and Zhang 2012). While hydrolytic hydrogenation of hemicellulose is an attractive alternative as hydrolysis and hydrogenation reactions are simultaneously promoted, it more easily leads to a wider range of products and controlling selectivity may be a sensitive task. Moreover, conversion does not take place at $H_2$ pressure below 50 bar (Arcaño et al. 2020).

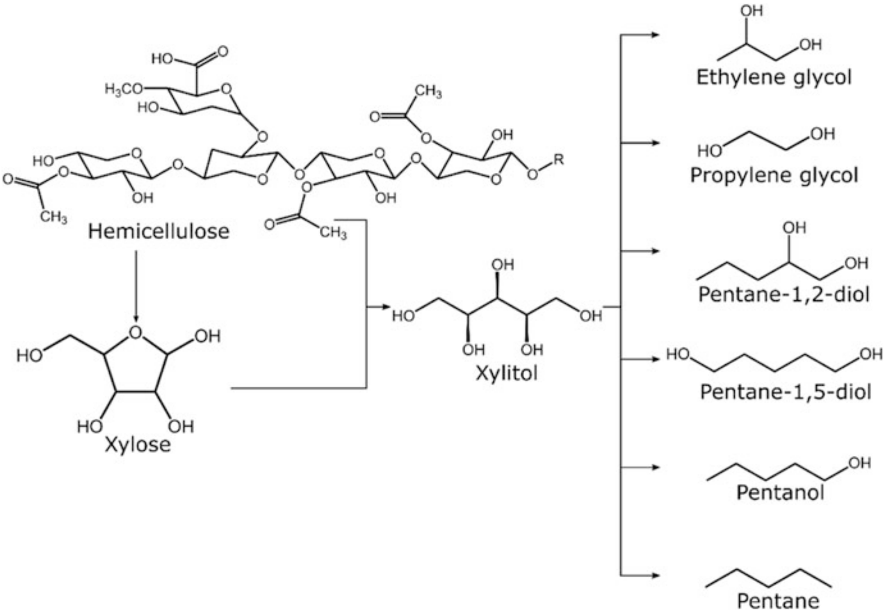

**Fig. 12.3** Pathways towards hemicellulose-based polyols

Considering the carbon backbone of hemicellulose sugars, xylitol is the one more readily obtained due to the chemical composition of hemicelluloses. In contrast, ethylene glycol and propylene glycol are the most wanted drop-in compounds potentially produced from pentoses. These three chemicals will be discussed herein to exemplify the feasibility of green production of polyols from hemicelluloses.

### 12.3.1 Xylitol

Xylitol is a food low-calorie sweetener that has been increasingly demanded due to its attractive properties. It is widely soluble in water, presents a sweetness capacity that exceed by around 20–25% that of sucrose and with no insulin requirement, turning it into a sugar substitute for diabetics (Benahmed et al. 2020). Furthermore, it is a dental caries reducer and therefore identified as a sugar alternative for candies and in confectionary (Zacharis 2012). It is indeed expected that xylitol application in food and confectionary segments may help to deal with the growing problems of oral health within children and adults. It should also be mentioned the use of xylitol in pharmaceuticals and personal care and cosmetics due to its emollient and humectant properties. All these segments are growth drivers for xylitol market, which globally surpassed USD 880 million in 2019 and is expected to grow in the years to come (Ahuja and Mamtani 2020).

Xylitol is currently produced through reduction of xylose released mostly from corncob hydrolysis (Feher et al. 2018) and there is no fossil feedstock-based alternative (Arcaño et al. 2020). This is a three-phase catalytic hydrogenation promoted over Raney nickel. This catalyst is indeed a very active system leading to high selectivity towards xylitol (Wisniak et al. 1974a, b; Mikkola et al. 2000, 2001; Hoffer et al. 2003). Despite relying on a low-price catalyst, the high price of xylitol comes from a costly, energy-intensive industrial process (Liu et al. 2019) since reaction is performed at hydrogen pressure within 20–50 bar and temperatures around 80–120 °C (Sifontes et al. 2010; Tathod and Dhepe 2014; Murzin et al. 2015a). Furthermore, some technical drawbacks have been driving the efforts to develop a more sustainable process alternative.

Raney nickel catalyst is easily deactivated upon xylose hydrogenation either via metal leaching or deposition of reaction by-products on the active surface sites (Mikkola et al. 1999a, b, 2000, 2001; Mikkola and Salmi 2001). Leaching nickel ions to the reaction medium is of major concern for food, personal care and pharmaceuticals uses due to the known toxicity of nickel ions. Besides the catalyst weight loss, there is a need for very restrictive downstream purification processes to ensure the final purity of the xylitol solution. By-product deposition onto catalyst surface, on the other hand, requires regular regeneration operations that will also impact the catalyst lifetime and the process economics due to the high energy demand.

Some strategies have then been investigated to overcome those issues, pushing towards more stable and recyclable catalyst-based technologies. Herein they are organized within three more relevant approaches:

- Catalysts obtained from pre-defined well organized precursor structures;
- Noble metal-based catalysts;
- Bimetallic catalytic systems.

#### 12.3.1.1 Catalyst Precursor Structure

Advanced catalyst surface architectures have been pursued by using some specific structures as Ni-based catalyst precursors. In this approach, distinct topology and flexible crystalline structures have been exploited, especially layered double hydroxides (Chen et al. 2017), phyllosilicates (Bian and Kawi 2020; Du et al. 2021) and perovskites (Morales et al. 2016, 2017, 2018). These precursor structures, represented in Fig. 12.4, all aim at building certain surface site assemblies that could improve chemical and structural stability of Ni active sites under xylose hydrogenation conditions. These bottom-up synthesis approaches have indeed been explored for a wide range of catalytic reactions as those precursor structures may lead to small, uniform particle sized tuned catalysts that could render notable catalytic behaviour.

Phyllosilicates have been recognized as a precursor structure able to lead to highly dispersed non-noble metal catalysts, especially those based on Ni, Cu, Co and Fe, which have revealed high stability and improved activity comparable in some cases to that of noble metal systems (Bian and Kawi 2020). Its use to prepare

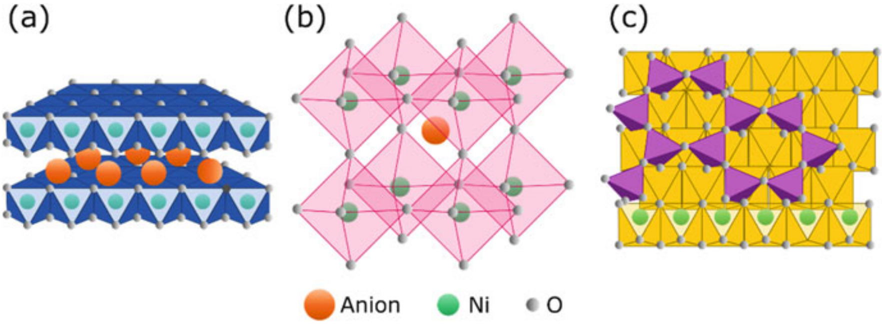

**Fig. 12.4** Structures of (**a**) layered double hydroxides, (**b**) perovskite and (**c**) phyllosilicate used as precursors for Ni-based catalysts synthesis

Ni-based catalysts for hydrogenating xylose to xylitol in water was only recently reported (Du et al. 2021). Nevertheless, many contributions can be found reporting the suitability of this precursor structure for reforming (Li et al. 2018a), hydrodeoxygenation (Yang et al. 2019), methanation (Zhao et al. 2017), Fischer–Tropsch synthesis (Park et al. 2017) and $CO_2$ hydrogenation (Richard and Fan 2017) reactions, though all in the gas phase.

Catalysts derived from phyllosilicates were more active for xylose hydrogenation than those obtained by conventional impregnation. Du et al. associated this performance to the higher Ni dispersion accomplished from the phyllosilicate precursor structure (Du et al. 2021), whose average metal sizes were around 6 nm against 27 nm for the impregnated catalyst. They also disclosed that no evident sintering occurred upon aqueous hydrogenation with only a negligible metal leaching. Such improved stability was ascribed to the strong interaction between Ni and silica support promoted by the phyllosilicate precursor. Remarkable liquid-phase hydrogenation activity of phyllosilicate-derived Ni catalyst with no apparent leaching was also reported by Wang et al. (2018).

The group of Pecchi has focused their investigation on perovskite structures as a way to stabilize Ni nanoparticles for aqueous-phase hydrogenation of xylose to xylitol at 100 °C under 25 bar $H_2$ pressure (Morales et al. 2016, 2017, 2018). The $ABO_3$ general formula of perovskites allowed the authors to vary the final catalyst composition while holding a Ni content of 20 wt.% ensured by the alongside addition of Al in the perovskite B position. Stabilization of the Ni-based catalysts in aqueous medium reaction was targeted by using A-site substitution with lanthanides (La, Ce or Nd) and B-site doping with Rh. The obtained Ni catalysts exhibited outstanding leaching resistance as no Ni loss was detected when a perovskite structure was taken as catalyst precursor (Morales et al. 2016, 2018). It contrasted with a metal loss of 15% when the catalysts were obtained from ordinary parent mixed oxides despite their slightly higher selectivity towards xylitol (Morales et al. 2016). Embedding small amount of Rh (0.3 wt.%) in B-site increased the catalyst reducibility and led to higher xylose conversion and xylitol selectivity as disclosed by reaction kinetic data (Morales et al. 2017). These studies highlighted a simple, promising approach relying on a precursor perovskite structure to obtain Ni leaching-resistant heterogeneous catalysts that can be used for xylose aqueous-phase upgrading to xylitol.

#### 12.3.1.2 Noble Metal-Based Catalysts

Production of xylitol through both direct hydrogenation of xylose and hydrolytic hydrogenation of hemicelluloses can be promoted over noble metal catalysts. The extensive literature on this approach is motivated by the intrinsic higher resistance of noble metal to leaching in aqueous-phase processing. Catalyst formulation, however, differs if it is meant to be used in hydrolytic hydrogenation.

Process based on the straightforward upgrading of hemicelluloses (xylan, arabinoxylan, glucuronoxylan, galactomannan, glucomannan and xyloglucan) requires bifunctional catalysts at which acidic sites should be present along with metal centres since they play a leading role in hydrolysis step prior to sugar reduction. Indeed, when non-acidic oxides, such as silica, is taken as support, the heterogenous catalyst is combined with a mineral acid. Some studies on xylan conversion reached ~80% xylitol at 200 °C and 60 bar of $H_2$ over Ir-Re/$SiO_2$ system but $H_2SO_4$ was also added to the reaction medium (Liu et al. 2016b). Yi and Zhang (2012) had previously proposed the addition of HCl or $H_2SO_4$ to boost the performance of Ru/C in hemicellulose upgrading. The major technological drawback in these processes is the hazardous character of the mineral acids and their related environmental impact lessening the overall process sustainability. Furthermore, controlling product distribution is also challenging. High concentration of mineral acids invariably leads to a decrease in xylitol yields and pentanols or pentane may also be formed alongside (Liu et al. 2016b). Modifying the surface of non-acidic supports is a feasible way out. Actually, organofunctionalization of silica to obtain acidic organic-inorganic hybrids (Canhaci et al. 2017) or oxidizing the surface of carbon materials to generate acidic oxygen groups (Ribeiro et al. 2016) are common strategies when a multifunctional catalyst is demanded.

Supporting noble metals on intrinsic acidic materials, however, is a simpler strategy. Zeolites, modified molecular sieves, acidic oxides such as $Nb_2O_5$, and acidic resins are then common choices. Hydrolytic hydrogenation of arabinogalactan to galactitol and xylan to xylitol have been investigated on Ru/MCM-48 (Kusema et al. 2012) and Ru/HUSY (Murzin et al. 2015b) respectively, leading to 20–25% yields.

Some studies, however, have shown that metal catalysts whose supports are able to in situ generate protons via dissociative $H_2$ adsorption can also promote hydrolytic hydrogenation. In this mechanism, $H^+$ ions migrate to coordinatively unsaturated sites (Lewis acid sites) forming protonic acid centres able to play a role in the hydrolysis step. C based supports (carbon nanotubes, activated carbon and graphite) are the most common examples irrespective of the noble metal. Indeed Ru, Pt, Pd and Rh have led to 80% xylitol yield using xylan as feedstock as shown in the contributions by Ribeiro et al. (2016), Yamaguchi et al. (2016), Ribeiro et al. (2017) and Li et al. (2018b).

As for xylose hydrogenation, Wisniak et al. (Wisniak et al. 1974a, b) reported that the activity of noble metals follows the order Ru > Rh > Pd, disclosing that Ru is outstandingly active in basic and neutral pH solutions. Extensive literature is available exploiting the use of Ru for xylitol production from xylose since then. Its performance indeed stands out in several studies comparing to other noble metals. Ru nanoparticles decorated multiwalled carbon nanotubes rendered 85% yield of xylitol while other furan compounds were also observed over Pd and Rh-based catalysts (Perez et al. 2018). Even higher selectivity towards xylitol (~98%) was achieved when Ru decorated carbon foam (Pham et al. 2016). Perez et al. (2018) claimed that the product distribution pattern is associated with the presence of acidic oxygen functional surface groups on carbon-based supports, and their vicinity to metal sites, which would promote the xylose cascade conversion to furfuryl alcohol as a side reaction. The role played by the support is indeed quite relevant to determine product distribution as already outlined for the domino hydrolysis-hydrogenation reactions in the hydrolytic hydrogenation pathway either due to the intrinsic support acidic properties or the formation of protonic acidic sites upon $H_2$ dissociation.

Hernandez-Mejia et al. (2016) reported that the support structure can also influence xylose hydrogenation. Using $Ru/TiO_2$, the authors showed that a highly efficient catalyst is obtained when rutile $TiO_2$ is taken as support, leading to >90% yield of xylitol, which was ascribed to the lower Ru particle size (5–7 nm) when compared to the bigger particles formed on anatase $TiO_2$, which rendered a less active and non-selective catalyst. Selectivity pattern was rationalized by the interaction of $Ti^{3+}$ species formed onto anatase-supported catalyst with the C-O bond driving its cleavage to glycols, as glycerol and ethylene glycol were produced alongside dropping xylitol selectivity. The effect of support polymorphs, such as rutile/anatase $TiO_2$ and monoclinic/tetragonal $ZrO_2$, has indeed been reported for different catalytic reactions (Franchini et al. 2012; Sato et al. 2013).

#### 12.3.1.3 Bimetallic Catalytic Systems

Despite the effectiveness of noble metals to overcome those shortcomings of using Ni-based catalysts, the fact that they are more expensive, may be impacted by fluctuating costs, and are also consumed by high technology markets drive the search for some feasible alternatives. The most pursued one is the formulation of bimetallic systems that can allow cost reduction while satisfying activity and stability requirements in water. Using bimetallic catalyst is also another strategy investigated to surmount the hydrothermal stability problems of lower-priced Ni catalysts.

Mikkola et al. investigated Mo-promoted Raney nickel catalyst in the hydrogenation of xylose to xylitol (Mikkola et al. 2000). However, catalyst modification with Mo did not bring about any benefit since a severe deactivation still took place. The authors accredited the drop of surface area and Mo leaching as the main reasons for deactivation. Catalyst deactivation kinetics disclosed, however, that deactivation was faster in aqueous than in aqueous ethanol solvent (Mikkola et al. 2000).

Incorporation of Re in Ni-based catalysts has also been evaluated by some researchers. Xia et al. supported bimetallic catalysts with different Ni/Re ratios on activated carbon (Xia et al. 2020). Small nickel particle sizes as well as the synergistic effect between Ni and Re were associated with the outstanding performance, reaching a xylitol yield of 98% at 140 °C. Nonetheless, Ni leaching was still observed even though the presence of Re decreased its extension.

Ni (Lee et al. 2014; Yadav et al. 2012), Co (Lee et al. 2014), Fe (Lee et al. 2014), Sn (Tathod and Dhepe 2015) and Ag (Paun et al. 2017), amongst other metals, have been studied as promoters for supported noble metal catalysts. It has been shown that the activity of bimetallic catalysts can be 110 times higher than monometallic ones for the aqueous-phase hydrogenation of carbonyl groups. Nonetheless, as regarding xylose hydrogenation, Lee et al. disclosed that the addition of Ni, Co or Fe on Ru, Pd or Pt catalyst renders no system more active than monometallic Ru supported catalyst (Lee et al. 2014). Furthermore, the modification of noble metal catalysts with some base metals may increase the rate of C-C cleavage reducing the selectivity to xylitol, as shown on Pd-Fe supported bimetallic systems (Lee et al. 2014).

The literature on this bimetallic approach suggests that controlling metal particle size and the surface properties of the support in the formulation of monometallic catalysts can be more effective for aqueous-phase polyols production from hemicellulose sugars.

### 12.3.2 Ethylene Glycol and Propylene Glycol

Hydrogenolysis of C5 sugar alcohols allows the production of lower carbon chain polyols analogous to those obtained from oil industry and some are also depicted in Fig. 12.3. These polyols are industrially relevant as they are used to produce polyurethanes, polyesters and polyethers, whose end-use and market include foams, insulators, adhesives, coatings and sealants widely used in the automotive, textile and packing segments.

Processes yielding ethylene glycol and propylene glycol from xylitol are performed at much harsher conditions if compared to xylose hydrogenation or hemicellulose hydrolytic hydrogenation to xylitol. Temperatures in the range 190–250 °C and $H_2$ pressures typically within 40–120 bar are needed to accomplish reasonable yields. Reaction conditions are indeed quite relevant when upgrading hemicellulose sugars to polyols as they can drive product distribution for a similar catalytic system. These information on reaction conditions are systematized in Fig. 12.5.

An alkaline reaction medium, usually provided by the addition of earth alkaline hydroxides, is also necessary as a way to promote retro-aldol condensation reaction (Rivière et al. 2017). Due to the already mentioned disadvantages of using a homogeneous co-catalyst, much effort has been spent to develop a base-free process.

Cu and Ni are interesting less costly metals for hydrogenolysis catalyst formulation since they are effective to cleavage C-O and C-H bonds, respectively (Li et al. 2019). Their susceptibility to leaching, however, is a challenge but then those

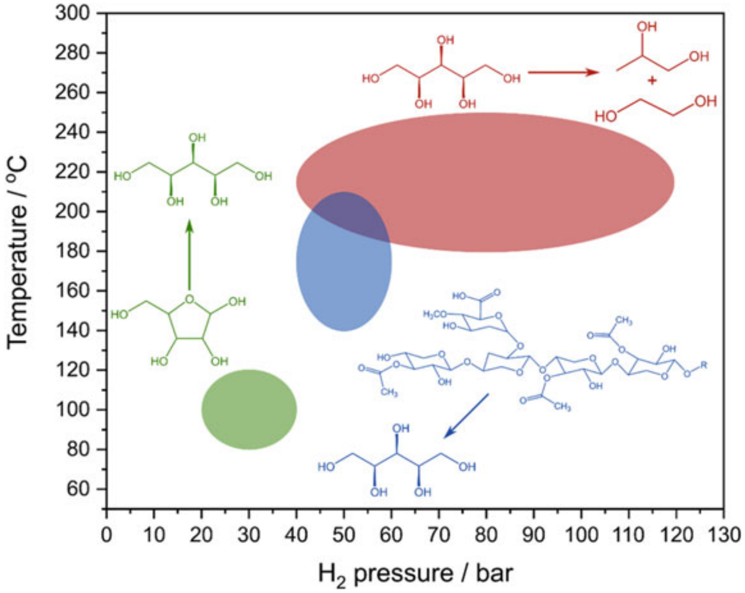

**Fig. 12.5** Operation conditions typically applied for polyols production from hemicellulose and hemicellulose-derived compounds

already discussed strategies regarding the catalyst precursor structure can again be a feasible solution.

Glycols yields of 62–67% can be obtained over supported Ni catalysts operating at 200–240 °C and 40–50 bar (Sun and Liu 2014; Zhou et al. 2015). By using Cu catalysts instead, slightly lower yields of glycols are accomplished, being within 66–70% as reported by Liu et al. (2014) and Zhu et al. (2016). Cu catalysts, however, require higher pressures (50–60 bar) while keeping the temperature in the same range. Remarkable 81% yields of glycols were reported when applying a bimetallic Ni-Cu catalyst under similar reaction temperature (200 °C) but even higher $H_2$ pressure (80 bar) (Liu et al. 2018b). Lower pressures at higher temperature (245 °C) did not lead to more than ~44% yields (Li et al. 2019). Liu et al. associated the good performance of the bimetallic catalysts with the formation of a Ni-Cu alloy phase, which decreases catalytic activity while improving the solid stability (Liu et al. 2018b). Such stability is a consequence of the preservation of Ni-Cu alloy with no important evolution to separate $Cu^0$ and $Ni^0$ phases.

Noble metal catalysts also present potential performance for producing glycols from xylitol. It is generally related to their activity to cleavage C-C bonds, being Ru the most promising metal phase. When supported on carbon (Ru/C), glycols yield reached around 50% in the presence of $Ca(OH)_2$ (Sun and Liu 2011), but it was notably pushed up to 70% when MnO was added to the catalyst formulation (Rivière et al. 2018). This modification also allowed to run the reaction in a base-free condition but in a water-methanol as solvent mixture. The presence of methanol was crucial to improve the formation of glycols as only 22% yield was accomplished when using just water under exact the same reaction conditions (Rivière et al. 2017).

Despite the higher activity, the main disadvantage of using noble metal catalysts, besides their higher cost, is the formation of chemicals other than glycols. Indeed, lactic acid, butanediol and methane are usually reported, reaching yields more significant if compared to the performance of non-noble Ni- or Cu-based catalysts.

Hydrogenolysis of xylitol is probably a central technology towards fossil-analogous low carbon glycols, which may allow building a bio-based chain for polyesters, plasticizers, anti-freeze and cosmetics. More efforts are still need in that direction, particularly regarding kinetic modelling, which is very relevant to the development of a feasible technology but are still missing in the literature.

## 12.4 Carboxylic Acids

Carboxylic acids are interesting compounds due to its vast application in food, chemical, pharmaceutical industries, amongst others. Another important usage of carboxylic acids is in the production of polymers, that used to be entirely dependent on fossil sources, that are not sustainable, renewable and environmentally friendly. Due to these drawbacks, the use of lignocellulosic biomass as feedstock to obtain carboxylic acids has been attracting attention recently.

Lots of different organic acids can be produced from the hemicellulosic fraction. In this section, two carboxylic acids that are well known for being important platform chemicals are addressed. They can both be obtained from hemicellulose-derived pentoses, one keeping the C5 backbone (levulinic acid) and the second derived from the cleavage of the C-C bond, generating a C3 organic acid (lactic acid).

### 12.4.1 Levulinic Acid

Levulinic acid is an excellent platform chemical to obtain various bio-based compounds due to its reactive structure. It also has vast application in the manufacturing of polymers, resins, solvents, fuel additives, plasticizers, pharmaceuticals, herbicides, flavouring agents, surfactants and anti-freeze agents (Rackemann and Doherty 2011).

The production of levulinic acid is a multi-step process based on the hydrolysis of lignocellulosic biomass, followed by the dehydration of monosaccharides (hexoses) into 5-hydroxymethylfurfural (HMF) and then its hydration to levulinic acid (Yan et al. 2015; Gallezot 2012). In this route, formic acid is produced alongside. Moreover, pentoses obtained from hemicellulose fraction can also be converted into levulinic acid. In this case, the pentose is firstly dehydrated to furfural, followed by its metal-catalysed hydrogenation to furfuryl alcohol, which is then hydrolyzed in acid media to levulinic acid (Yan et al. 2015; Climent et al. 2014) as shown in

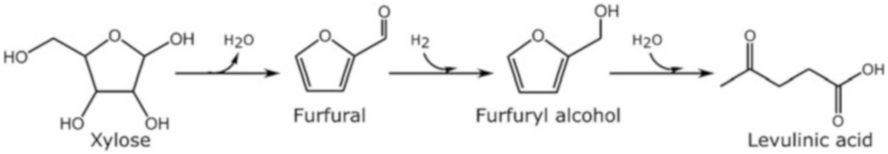

**Fig. 12.6** Simplified pathway for levulinic acid production from xylose

Fig. 12.6. Only the pentose-based pathway will be discussed herein due to the particular focus on hemicellulose biorefinery.

#### 12.4.1.1 Xylose Direct Conversion

Xylose conversion into levulinic acid is a complex process since it involves multiple steps and different kinds of reactions that, consequently, need different conditions and catalysts properties. So far, there are not many studies in the literature related to the direct conversion of xylose to levulinic acid.

Hu et al. used a combination of an acidic solid catalyst (Amberlyst 70) and a metal hydrogenation catalyst ($Pd/Al_2O_3$) to convert xylose into levulinic acid/alkyl levulinate (Hu et al. 2013). The maximum product yield obtained was around 23% working at 165 °C and 70 bar of $H_2$. It is not a viable system as it rendered low yield and still use a noble metal catalyst and molecular hydrogen, which are expensive. As a consequence, the same group later promoted xylose one-pot conversion into levulinic acid/esters in a simpler process at which an acid catalyst (Amberlyst 70) and a dimeth/methanol medium were necessary (Hu et al. 2017). Despite the higher yields of alkyl levulinate (~50%), it is still not sufficient for an industrial application.

Later on, Shao et al. evaluated the efficiency of beta zeolite based catalysts to promote xylose conversion to levulinic esters (Shao et al. 2019a). Different metal ions (Zr, Ni, Fe and Sn) were investigated as zeolite modifiers, and Zr-beta catalyst showed the best performance. The authors then changed the calcination temperature and Zr content and noticed that by increasing calcination temperature also increased levulinic acid/ester yields. This trend was concluded to be associated with the consequent decrease in the concentration of Brönsted acid sites, which are responsible for furfural polymerization. Increasing Zr content also increased levulinic acid/esters yield, up to a maximum value. The best performance of Zr-beta catalyst, with yields of ~92% of levulinic acid/ester, was obtained at 190 °C and reactant/solvent ratio 0.25/9.75 wt./wt. (Shao et al. 2019a). Recently, Zr was also evaluated over MCM-41 in a dual catalyst system, but only 53% of alkyl levulinate was obtained (Wang et al. 2020).

#### 12.4.1.2 Furans Conversion

Levulinic acid can be obtained from the hydrolysis of furfuryl alcohol, which is catalysed by Brönsted acid solids. However, furfuryl alcohol is a high reactive molecule and when in acidic medium tends to polymerize, forming humins and rendering low product yields (Mellmer et al. 2015). In a way to overcome these issues, furfuryl alcohol conversion usually takes place in an alcoholic medium, that ends up forming alkyl levulinates. There are a lot of reports about alcoholysis of furfuryl alcohol in the presence of different acidic catalysts, for example, zeolites, resins, heteropolyacids, $Al_2O_3$/SBA-15, sulphated $TiO_2$ and organic-inorganic hybrid catalysts (Shao et al. 2019b; Sankar et al. 2017; Zhao et al. 2018; Enumula et al. 2017; Zhang et al. 2011; Lange et al. 2009).

Recently, Vaishnavi et al. made a detailed study about the role of zeolites active sites in the alcoholysis of furfuryl alcohol to alkyl levulinates (Vaishnavi et al. 2021). In this study the author noticed that the catalysts pore size has a great influence on catalyst efficiency since large pore zeolites (Beta and Y) were not as efficient as ZSM-5 to convert the reaction intermediates (butoxy methyl furan) into butyl levulinate. Different Si/Al ratios were evaluated and butyl levulinate selectivity increased along with the Si/Al, in the order of SAR95 > SAR117 > SAR160 > SAR57 > SAR22 (Vaishnavi et al. 2021). The authors justified that at lower Si/Al oligomers are more favourably formed due to the high Brönsted acidity; yet, at higher Si/Al the lower concentration of acid sites decreased the catalytic activity. After some adjustments in the reaction conditions in order to optimize the process, ZSM-5 zeolite proved to be an interesting catalyst for the alcoholysis of furfuryl alcohol into alkyl levulinates, showing great activity and selectivity in 24 h of reaction and exhibiting reusability up to four cycles.

Alcoholysis of furfuryl alcohol provides a simpler pathway to obtain alkyl levulinates where a Brönsted acid catalyst is needed. However, the one-pot conversion of furfural into alkyl levulinates is more complex, where first furfural must be hydrogenated to furfuryl alcohol, which normally occurs in the presence of molecular hydrogen and metal catalysts, as already previously discussed in this chapter. On the other hand, there is also the possibility of hydrogenating furfural into furfuryl alcohol without using molecular hydrogen and metal-based catalyst, through the Meerwein–Ponndorf–Verley (MPV) reduction. For this system, a catalyst possessing Lewis acid sites and an alcohol functioning as a hydrogen donor is demanded. Therefore, the catalyst formulations get a little more complex since it now needs to possess Lewis acid sites to promote furfural MPV reduction to furfuryl alcohol, followed by its alcoholysis over Brönsted acid sites.

In order to develop a greener and cheaper process, lots of reports recently focused on this approach and different catalyst holding both Brönsted and Lewis acid sites were studied (Li et al. 2020; Zhang et al. 2020; Ye et al. 2020; Peng et al. 2021; Nandiwale et al. 2021). Some authors have tried to tune the Brönsted/Lewis acid sites ratio to achieved a better catalyst performance (Li et al. 2020; Ye et al. 2020). In most cases, alkyl levulinates yields higher than 70% was obtained, showing a promising way for furfural valorisation (Li et al. 2020; Zhang et al. 2020; Peng et al. 2021).

### 12.4.2 Lactic Acid

Lactic acid is extensively used in the industry, particularly in the food, cosmetics, textile and pharmaceutical segments. It is also a building block for the production of

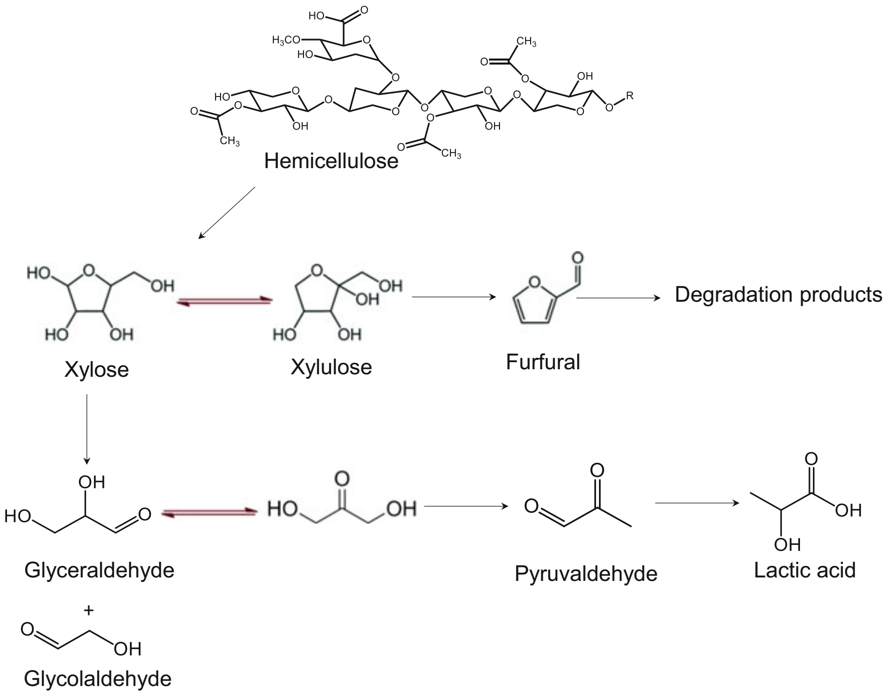

**Fig. 12.7** Pathways for lactic acid production from hemicellulose fraction

green solvents and biodegradable polymers, like alkyl lactates and polylactic acid (PLA) (Liu et al. 2020; Mäki-Arvela et al. 2014; Bozell and Petersen 2010). Traditionally, lactic acid is produced by a biotechnology process via carbohydrates (mainly glucose and sucrose) fermentation (Dusselier et al. 2013). However, there are numerous disadvantages related to this process like, low reaction rate, demands high energy, does not produce pure lactic acid and at the end of the process tons of gypsite waste are generated from the neutralization step (Dusselier et al. 2013; Bozell and Petersen 2010). Alternatively, lactic acid is also obtained through chemical synthesis based on the lactonitrile hydrolysis, propionic acid hydrolysis and reaction between acetaldehyde, carbon monoxide and water (Martinez et al. 2013; John et al. 2007; Datta et al. 1995). These technologies present some important disadvantages as reactions are usually performed under drastic hazardous conditions.

Chemocatalytic production of lactic acid might be a better option, since it can work with cheaper raw material (lignocellulosic biomass) and can allow higher reaction rates. There are several recent reports focusing on the direct conversion of cellulose or glucose into lactic acid/alkyl lactates (Marianou et al. 2019; Deng et al. 2018; Wattanapaphawong et al. 2017a, b; Wang et al. 2013). Upgrading hemicellulose or hemicellulose-derived monosaccharides, however, are still vastly outnumbered (Kim et al. 2020; Xu et al. 2020b; Paulino et al. 2018; Yang et al. 2015).

Hemicellulose direct conversion into lactic acid/alkyl lactates is complex, full of different reaction steps and can lead to many by-products, as depicted in Fig. 12.7, depending on the reaction conditions and catalysts used. Furthermore, most processes are promoted by homogeneous catalyst or biocatalysts (Kim et al. 2020; Xu et al. 2020b). The possibility of using hemicellulose as feedstock is, however, feasible as easily observed by the numerous reports dealing with hemicellulose-derived molecules into lactic acid/alkyl lactates, such as trioses (dihydroxyacetone and glyceraldehyde) and xylose, which will both be addressed herein.

#### 12.4.2.1 Conversion of Trioses

Triose conversion into lactic acid/alkyl lactates is a two-step process starting from sugar dehydration to pyruvaldehyde followed by a rearrangement via a hydride-shift mechanism with addition of water, leading to the formation of lactic acid, or alcohol molecule, forming alkyl lactates (Nakajima et al. 2018; Pescarmona et al. 2010; Taarning et al. 2009). The use of an alcoholic medium has been preferable since most heterogeneous catalysts studied in the presence of water suffered structural modifications and favoured the formation of carbonaceous deposits, which led to the catalyst deactivation (Santos et al. 2019; Nakajima et al. 2018; Clippel et al. 2012; West et al. 2010; Taarning et al. 2009.) Nonetheless, from a technological perspective, it is important to overcome the limitation of using water since a large amount of it is obtained after hemicellulose hydrolysis (Chen 2015). Hence, this section is focused on the recent studies that were specifically carried out in the presence of water.

The number of reports using water as a sole solvent is really inferior than the ones using an alcoholic medium and they have evaluated the performance of different zeolites, such as Y, ZSM-5, beta, USY and modernite, beta zeolite substituted with Zr, Sn and Ti ions, and Sn-MCM-22, tin phosphates, carbon-silica composites and metal oxides ($ZrO_2$, $TiO_2$ and $Nb_2O_5$) (Innocenti et al. 2020; Santos et al. 2019; Wang et al. 2015; Guo et al. 2013; Clippel et al. 2012; West et al. 2010; Taarning et al. 2009). In all cases, lactic acid selectivity was associated with the presence of Lewis acid sites, the ones responsible for the second step of the reaction, pyruvaldehyde hydride-shift. These sites have also been claimed to be active in dehydration step as observed by using Lewis metal oxides ($ZrO_2$ and $TiO_2$) but it well known that this reaction step is most favourable to occur over Brönsted acid sites. As it is common knowledge that Lewis acid sites are vulnerable in water, forming Lewis acid-water adducts, the development of catalysts exhibiting water-tolerant Lewis acidity is crucial.

Santos et al. evaluated the behaviour of different oxides in the transformation of triose into lactic acid in the presence of water. It was observed that lactic acid selectivity increased along to the amount of water-tolerant acid sites and showed the potential of $TiO_2$ and $Nb_2O_5$ as catalysts (Santos et al. 2019). However, since $TiO_2$ only possess Lewis acidity, its activity was way inferior to the one observed for $Nb_2O_5$, that holds both Brönsted and Lewis acid sites. The better performance of $Nb_2O_5$ was also reported by Nakajima et al. (2018). Consequently, $Nb_2O_5$ and Nb-based catalysts have caught the attention and recent works have been published using these materials for triose conversion into lactic acid (Innocenti et al. 2020; Wang et al. 2019, 2018). It was also reported that the structure of $Nb_2O_5$ can influence the concentration of water-tolerant Lewis acid sites; a deformed orthorhombic $Nb_2O_5$ structure presenting higher amount of water-tolerant Lewis acid sites than the non-crystalline niobic acid ($Nb_2O_5 \cdot nH_2O$) (Nakajima et al. 2018). However, only one $Nb_2O_5$ structure was evaluated so far and no further detail regarding this matter was published yet.

### 12.4.2.2 Pentoses Conversion

Yang et al. reported for the first time, in 2015, the direct conversion of xylose into lactic acid over $ZrO_2$ catalyst (Yang et al. 2015). Normally, basic catalysts would promote xylose retro-aldol condensation into a C3 and C2 compounds. Yang et al. (2015) proposed that both acid and basic sites were participating in the C-C cleavage over $ZrO_2$. This conclusion was corroborated by Paulino et al. (2018), who observed that xylose retro-aldol condensation was also dependent of the basic site strength on amphoteric oxides (Paulino et al. 2018). It was then proposed by both studies that the reaction would start by the monosaccharide adsorption on Lewis acid centres, which led to an increase of the positive charge of this carbonyl group, making it easier to undergo a nucleophilic attack. Both studies suggested that the C-C cleavage would happen between C2 and C3 positions. A recent work conducted by Zhang et al. over Sn-beta catalyst, however, claimed that the cleavage occurs between the C3 and C4 bonds (Zhang et al. 2020). The authors also showed that lactic acid was formed from erythrose in a parallel reaction. This tetrose would be formed from the polymerization of C2 compounds (glycolaldehyde).

A few more reports were recently published correlating xylose conversion to the catalysts Lewis acidity by using different catalysts, like metals supported on $\gamma$-$Al_2O_3$, ZSM-5 and MOFs (Kosri et al. 2021; Ponchai et al. 2020; Kiatphuengporn et al. 2020). One common point in all those reports is that Lewis acidic centres are needed to promote monosaccharides retro-aldol condensation reaction. Managing to take the reaction further until lactic acid demands the catalyst to present Brönsted acid sites as well to allow the dehydration of trioses into pyruvaldehyde and then producing lactic acid from pyruvaldehyde hydride-shift.

## 12.5 Summary and Outlook

Some important issues related to the production of high value products from hemicellulose were addressed in this chapter. Both drop-in chemicals and those compounds that are not currently obtained from the conventional petrochemical industry were highlighted. It is outlined that a stablished market for hemicellulose-derived green chemicals is a drive for the advance of new technologies in a biorefinery context. Nonetheless, a wide variety of chemicals can be obtained from hemicellulose, many with no market demand yet. The development of new applications is therefore mandatory for the hemicellulose biorefinery rise. This is particularly relevant in the near future at which vehicles electrification is expected with a consequent drop in biomass to biofuel production and hence forwarding waste biomass to bioproducts is quite strategic.

From the scientific point of view, it was made clear that technologies to convert hemicellulose to bioproducts must rely on aqueous-phase processing. Green solvents that can be easily separated from the final products should be taken whenever a water-based process is not feasible.

The requirement for converting hemicellulose in water solutions imposes close attention to the development of heterogeneous catalysts. Their structural and chemical stability and their surface properties in the presence of water, in special the surface acidity, are of major concern for catalyst design. Furthermore, the porous network has to be taken into consideration as confinement effects may promote catalyst deactivation. As a general trend, non-noble metal catalysts either as a monometallic or in a bimetallic system are desirable due to their lower cost and effectiveness for the reactions involved in hemicellulose upgrading. Their susceptibility to leaching can be overcome by exploiting some synthesis strategies, especially by using a catalyst precursor well defined structure.

Finally, it must be emphasized that there is still a need for new processes to thoroughly explore the transformation of hemicelluloses into bioproducts due to the vast possibilities of molecular structures. Studies devoted to reaction kinetics and use of continuous flow reactors are still scarce and thus highly demanded from the perspective of industrial application.

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# 13 Synthesis of Furan Compounds from Hemicelluloses

Huiying Liu, Qixuan Lin, Rui Li, Minmin Chang, and Junli Ren

## Abstract

Lignocellulosic biomass is regarded as a sustainable raw material that can produce various important chemicals and fuels. Hemicelluloses rank second to cellulose in lignocellulosic biomass, comprising roughly 1/4 to 1/3 of most plants. Generally, the two predominant hemicelluloses are xylan and mannan, in which xylose (pentose) and mannose (hexose) are the main sugar units, respectively. Furan compounds such as furfural and 5-hydroxymethylfurfural which could be derived from pentose and hexose are important platform chemicals for the preparation of biofuels, plastics, and pharmaceuticals. Herein, we attempt to provide overview of the synthesis for furfural and 5-hydroxymethylfurfural (5-HMF) from hemicelluloses. Especially, the design of catalyst and solvent effect would be highlighted for improving the reaction efficiency. Another important focus would be paid on the reaction mechanisms of furfural and 5-HMF. The major challenges and promising technologies would be proposed in view of industry.

## Keywords

Furfural · 5-Hydroxymethylfurfural · Catalyst · Solvent · Mechanism

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M. Brienzo (ed.), *Hemicellulose Biorefinery: A Sustainable Solution for Value Addition to Bio-Based Products and Bioenergy*, Clean Energy Production Technologies, https://doi.org/10.1007/978-981-16-3682-0_13

## 13.1 Introduction

Fossil resources are the main source for the synthesis of fine chemicals and fuel energy (Fig. 13.1). However, the development of fossil resources is faced with great challenges due to their unrenewable nature and environmental problems. In order to solve or reduce these problems, it will be a top priority to seek some sustainable resources that can replace the petroleum resources. Lignocellulosic biomass is regarded as a sustainable raw material because of its renewable property, high carbon content, and abundant distribution. It is mainly composed of hemicellulose, cellulose, and lignin. Cellulose, as the major structural polymer of plant cell wall, is a linear polysaccharide consisting of anhydro-D-glucose monomer units linked by glycosidic bonds. Hemicellulose is a branched polysaccharide comprised of different sugar monomers such as glucose, xylose, mannose, galactose, arabinose and uronic acids. Conversely, lignin is a complex, three-dimensional polymer of aromatic compounds connected by cross-linking via C-O-C ether bonds and C-C bonds (Pérez et al. 2002; Limayem and Ricke 2012). Various high value-added products and biofuels can be prepared from these three components (Rostrup-Nielsen 2005; Dodds and Gross 2007; Kapu and Trajano 2014), including liquid fuel (gasoline, diesel), gas fuel (biogas, hydrogen), furan chemicals (furfural and 5-hydroxymethylfurfural), organic acid chemicals (formic acid, levulinic acid), small molecular alcohols (methanol, ethanol), aromatic hydrocarbons, etc. Compared with the development of cellulose, the utilization of hemicellulose is relatively inefficient, mainly due to the complexity of its structure and diversity of properties. So, it is crucial to develop hemicellulose selective conversion methods to facilitate effective utilization of hemicellulose, avoiding adverse reactions of cellulose and lignin. Furan compounds, the downstream products derived from pentose and

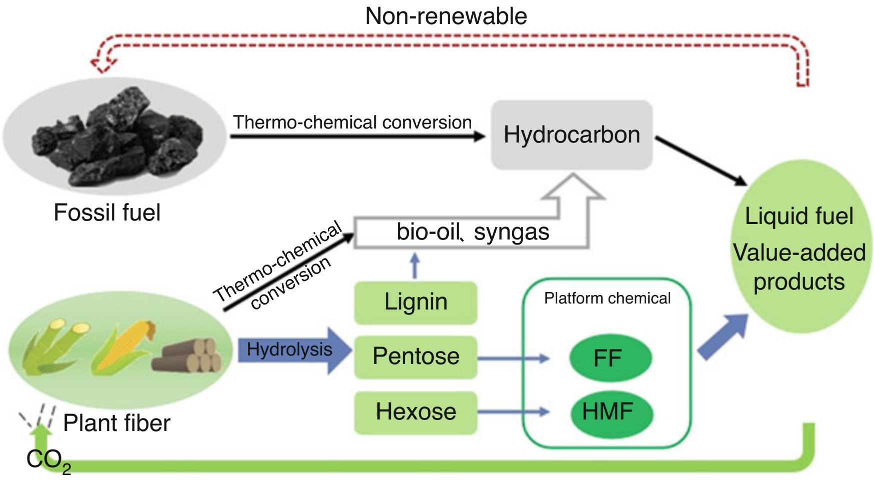


**Fig. 13.1** Synthesis of chemicals and fuels from lignocellulosic biomass

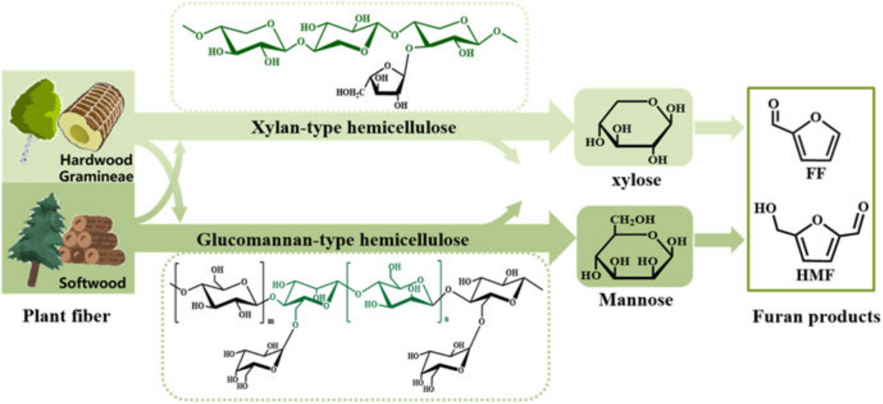


**Fig. 13.2** Selective conversion of hemicellulose into furan platform compounds

hexose of hemicellulose, are important platform compounds for the preparation of biofuels, polymers, pharmaceuticals, and others. This review mainly introduces the utilization of hemicelluloses for the preparation of main furan compounds, furfural and 5-hydroxymethylfurfural (5-HMF).

Furfural and 5-HMF are important platform compounds, can be derived into a range of liquid fuels and chemicals. Downstream products derived from furfural include furfuryl alcohol, furan, tetrahydrofuran, 2-methyltetrahydrofuran, cyclopentanone, succinic acid, maleic anhydride, levulinic acid, γ-valerolactone, etc.; downstream products derived from 5-HMF include 2,5-furaradiformic acid, 2,5-dimethylfuran, 5-ethoxymethylfurfural, levulinate, γ-valerolactone, etc. They are widely used in oil refining, plastics, medicine, agrochemical, and other industries, and are of great significance for replacing traditional petrochemical products and energy.

Hemicellulose is one of the main raw materials for the production of furan chemicals. The transformation of hemicellulose into target furan platform compounds can be simply divided into three steps, that is, hemicellulose is dissolved from feedstock; hemicellulose is hydrolyzed into monosaccharides; monosaccharides is dehydrated to produce target furan chemicals (Fig. 13.2) (Deng 2016).

## 13.2 Properties of Furfural

Furfural (2-furaldehyde, α-furfuraldehyde, furfural) was first discovered by Doebernier in 1821 (Dunlop and Peters 1953; Danon et al. 2013). Subsequently, the physicochemical properties and the synthesis methods of the compounds have been studied in depth. Pure furfural is a clear, colorless, oil-like liquid with an almond flavor. Exposed to light and air, it quickly turns yellow to reddish brown and tends to evaporate with steam. It is slightly soluble in water, easily soluble in

**Table 13.1** Physical properties of furfural

| Basic properties | Furfural |
|---|---|
| Molecular formula | $C_5H_4O_2$ |
| Molecular weight (g/mol) | 96.084 |
| Melting point (°C) | −36 °C (L) |
| Boiling point (°C) | 161.7 |
| Refractive index | 1.515 |
| Density (g/mL) | 1.0–1.2 |

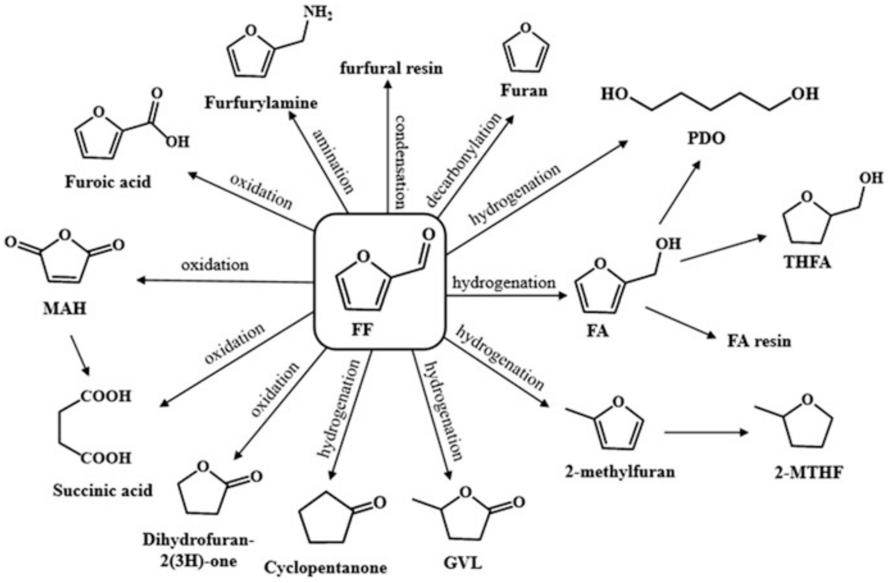


**Fig. 13.3** Furfural and its derivatives

organic solvents of aromatic hydrocarbon and unsaturated hydrocarbon such as ethanol, acetone, chloroform, ether, and benzene, and hardly soluble in saturated hydrocarbon. The physical properties of furfural are shown in the Table 13.1.

Furfural is one of the most important derivatives of furan compounds, which is recognized as one of the top 12 value-added products by the US Department of Energy (DOE) (Montané et al. 2002; Werpy and Petersen 2004; Jean-Paul et al. 2012). A furfural molecule has an aldehyde group and a dienyl ether functional group, so it can be hydrogenated, oxidized, chlorinated, nitrated, and condensed to produce more than 1600 derivatives because of its active chemical properties. As shown in Fig. 13.3, some important furan intermediate can be obtained through hydrogenation of furfural, such as furfuryl alcohol and tetrahydrofurfuryl alcohol, which can be further used to produce γ-valerolactone and 1,5-pentanediol, etc. Furfural can also be oxidized to form maleic anhydride, succinic acid, furoic acid, etc. Furfurylamine can be obtained through amination reaction, and a variety of high value-added products can be prepared by other reactions.

In 1922, American Quaker Oats Company first realized the industrialization of furfural, using oat hulls as raw material with $H_2SO_4$, and the furfural was mainly used in wood rosin decolorization and lubricating oil refining (Brownlee and Miner 1948). In the 1940s, furfural was widely used in synthetic rubber, medicine, pesticides, and other fields. After the 1960s, the development of furfural derivatives, especially the wide application of furan resin in the foundry industry, greatly promoted the development of furfural industry (Dias et al. 2010). At present, furfural has been identified as one of the most promising chemical platforms derived exclusively from biomass (Monroe 1921; Bariani et al. 2020). It is a renewable and green chemical product and widely used in oil refining, plastics, medicine, and pesticide industries (Bozell and Petersen 2010; Mariscal et al. 2016).

Furfural production in China began in the late 1930s and developed in the 1950s (Nie et al. 2019a). At present, China is the country with the largest furfural production in the world (70% of the total global production) (Mamman et al. 2008). By the end of December 2015, there were more than 260 furfural production enterprises and 28 furfural alcohol production enterprises in China, and the actual annual output of furfural in China was around 210,000 tons. Since 2017, the Ministry of Environmental Protection has stepped up pollution inspection, with most of the enterprises shutting down due to inadequate environmental protection facilities. In 2019, there were 162 furfural enterprises in China, with a total annual production of about 685,000 tons (Feng et al. 2019).

Industrially, furfural is obtained from lignocellulosic biomass under the catalysis of dilute acids (sulfuric acid, hydrochloric acid, phosphoric acid, and acetic acid), and the most commonly used catalyst is dilute sulfuric acid. More than 95% of furfural production enterprises in China adopt sulfuric acid catalysis method, using 3–6% diluted sulfuric acid as catalyst, and a few use hydrochloric acid as catalyst. The raw material (mainly corncob) and catalyst were firstly cooked at high temperature (140–185 °C) and under high pressure (3.5–10 atm) for 3–10 h. Furfural was then recovered from the liquid phase by steam stripping to avoid further degradation and purified by double distillation. With further refining and purification, pure furfural was obtained. However, a furfural yield of only 45–55% was obtained (Gao et al. 2010). The waste residue (mainly cellulose and lignin) collected can be used as boiler fuel to produce steam.

## 13.3 Influencing Factors of Furfural Production

There are many factors influencing the preparation of furfural, such as raw materials, solvent system, catalyst, furfural separation method, heating method. All these factors affect the yield and purity of furfural, which need to be considered comprehensively. In this section, the influencing factors of furfural production are summarized and classified, and the more detailed information about how these factors influence the furfural production is expounded in the next section.

### 13.3.1 Raw Material

Furfural is formed by dehydration and cyclization of pentose, which is hydrolyzed by pentosan in the presence of acid. The content of pentose in different biomass is different due to the type of hemicellulose. The main hemicellulose components in softwood, hardwood, and gramineae are galactoglucomannan, glucuronoxylan, and arabinoxylans, respectively (Peng et al. 2012; Carvalho et al. 2019). Therefore, the preparation of furfural from hardwood and gramineous plants is better than that from softwood. In China, the reserves of gramineae are abundant, such as corncob, bagasse, and rice straw. The theoretical furfural productions of per gram corncob, sugarcane bagasse, corn straw, sunflower shell, rice husk, and hardwood are 0.22 g, 0.17 g, 0.165 g, 0.16 g, 0.12 g, and 0.15–0.17 g, respectively (Montane et al. 2002; Ebringerová et al. 2005; Gírio et al. 2010). Among them, the content of hemicellulose (pentosan) in corncob is the highest (39–43%), and the theoretical furfural production is also the highest (Montane et al. 2002; Pu et al. 2016; Arai et al. 2019). Therefore, in China, corncob is the most common raw material used in the production of furfural. Table 13.2 summarizes the commonly used raw materials for furfural preparation.

### 13.3.2 Solvent System

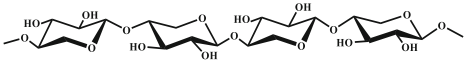
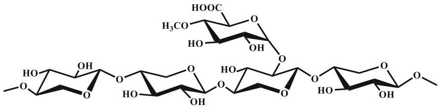
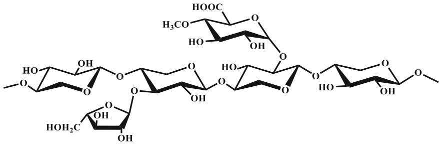
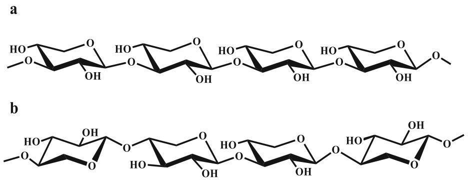
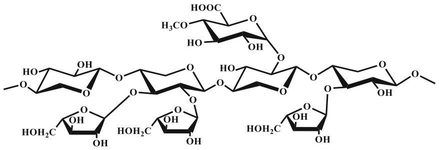
Solvents play an important role in catalytic reactions. Solvent can affect the solubility, mass transfer, stability of transition state, product distribution and yield, as well as the behavior of catalyst, and ultimately affect the reaction rate, reaction equilibrium, and reaction mechanism (Lin 2020). The solvent system during furfural production can be divided into monophasic system and biphasic system. The monophasic system is composed of a single solvent or a mixture of mutually soluble solvents; the biphasic system consists of a reactive phase and an organic phase (extractive phase).

#### 13.3.2.1 Monophasic System

The monophasic system is commonly used in industrial production, in which the crude furfural is extracted from the reaction vessel by steam stripping, and the furfural with higher purity can be obtained by further distillation and purification (Dunlop and Peters 1953). In the monophasic system, the reaction medium can be water, ionic liquid, supercritical $CO_2$, or organic solvents such as dimethylsulfoxide (DMSO), γ-valerolactone (GVL), and *N*,*N*-dimethylacetamide (DMA), γ-butyrolactone (GBL), *N*,*N*-dimethylformamide (DMF), etc. Table 13.3 summarizes the classification of monophasic system in furfural production.

Water is the most environmentally friendly solvent and is one of the most commonly used reaction media during the furfural production. On the other hand, water is the great medium to dissolve sugars (reactant). Various contents of xylose could be dissolved in water (466.5 g/L), DMSO (296.9 g/L), DMF (69.8 g/L), methanol (15.0 g/L), isopropanol (2.9 g/L), GVL (2.7 g/L), tetrahydrofuran (2.6 g/

**Table 13.2** Summarization of raw materials in furfural production

| Xylan-type hemicellulose | Structure (Heinze and Liebert 2012) | Example (Carvalho et al. 2019) |
|---|---|---|
| β-(1 → 4) Xylan |  | Grasses: corncob (Pu et al. 2016) |
| 4-*O*-Methyl-Glucuronoxylan (MGX) |  | Hardwoods: birch and eucalyptus |
| (Arabino)glucuronoxylan (AGX) |  | Grasses: bamboo stalk; Softwoods: spruce |
| Xylan<br>a: β-(1 → 3)<br>b: β-(1 → 3, 1 → 4) |  | Algas: red seaweeds (Deniaud et al. 2003; Fukuyama et al. 2005) |
| Water-soluble (Glucurono)arabinoxylan (GAX) |  | Grasses: sugarcane bagasse, sugarcane straw |

(continued)

**Table 13.2** (continued)

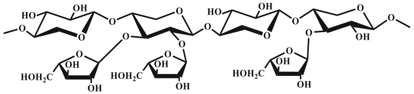
| Xylan-type hemicellulose | Structure (Heinze and Liebert 2012) | Example (Carvalho et al. 2019) |
|---|---|---|
| Water-soluble arabinoxylan (AX) |  | Cereals: wheat, oat, rice, corn |

**Table 13.3** Classification of monophasic system in furfural production

| Classification | | Example | Reference |
|---|---|---|---|
| Single solution | $H_2O$ | $H_2O$ | Lin et al. (2020) |
| | Organic solvent | DMSO, GVL, DMA | Wang et al. (2014c), Li et al. (2017a) |
| | Ionic liquid | BMImCl | Zhang et al. (2013) |
| | Supercritical fluid | Supercritical $CO_2$ | Games et al. (1997) |
| Co-solution | Organic solvent-$H_2O$ | DMSO-$H_2O$, Ethanol-$H_2O$, GBL-$H_2O$, GVL-$H_2O$ | He et al. (2016), Luo et al. (2017) |
| | Organic solvent-IL | MIBK-[BMIM]$HSO_4$ | Peleteiro et al. (2016a) |

L), acetone (2.4 g/L), and GBL (2.1 g/L) (Lin et al. 2020). Compared with organic solvents, water can dissolve much more xylose. $H_2O$ was also proved to selectively promote the cleavage of the intermolecular linkages between cellulose, hemicellulose, and lignin, and the cleavage of β-(1,4)-glycosidic bonds in hemicellulose at 160 °C (Luo et al. 2018). However, in the pure water system, the yield of furfural is lower than 50%, and high pressure is needed as the boiling point of water is lower than the reaction temperature. Moreover, the high polarity of water will result in some side reactions. Co-solvents such as DMSO, GVL, and GBL can be added into the aqueous solution to improve the reaction efficiency. Some researchers have found that GBL and GVL, as green solvents, have a weaker affinity with xylose than DMSO, DMF, and isopropanol, but a stronger affinity with furfural. Therefore, GBL and GVL could provide a protective shell for furfural and effectively inhibit the side reactions of furfural (Lin et al. 2020). Additionally, Luo et al. found that the oxygen in the ring of GVL might interact with hydroxyl groups of xylose unit to enhance the dehydration of xylose to furfural (Luo et al. 2018). In GVL, the activation energy barrier for xylose dehydration was decreased, whereas the barrier for furfural degradation was higher compared to water, leading to a significant increase in the reaction rate and furfural selectivity (Mellmer et al. 2014). DMSO could stabilize the positively charged intermediates of xylose and therefore restraining the condensation of xylose and furfural (Dias et al. 2006a). Ionic liquids (ILs) have low volatility, good solubility, good chemical and thermal stability, non-flammability, non-toxicity, recyclability (Olivier-Bourbigou et al. 2010; Peleteiro et al. 2016a, b). Specific ILs can improve catalyst activity and reaction selectivity compared with traditional solvents, and are suitable for furfural production (Lima et al. 2011). However, there are still some problems of ionic liquids, such as expensive, difficult to produce and recycle.

Although the monophasic system is more commonly used, the products in the hydrolysate are complex and prone to side reactions among each other, so the purity of furfural is not high. Besides, most of the organic solvents (such as DMSO, GVL, and DMA) have higher boiling points, which is not conducive to the separation and purification of furfural (Wang 2015; Nie et al. 2019b).

### 13.3.2.2 Biphasic System

In the biphasic system, furfural was hydrolyzed in aqueous phase and then extracted into organic phase to avoid the side reaction of furfural, which improve the yield and selectivity of furfural. Solvents such as water and ionic liquid, which are commonly used in monophasic system, are used as the reaction phase, and 2-butanol, toluene, methyl isobutyl ketone (MIBK), tetrahydrofuran (THF), cyclopentyl methyl ether (CPME), 2-methyltetrahydrofuran (2-MTHF), dichloromethane (DCM), 2-sec-butylphenol (SBP), and other water-immiscible organic extractants are generally used in the organic phase (Table 13.4) (Li et al. 2015a; Lin 2020).

The distribution coefficient (*R*) of furfural, that is, the ratio of furfural concentration in the organic phase to the aqueous phase by the same volume, is one of the important indexes for measuring the biphasic system. The *R* value can reflect the extraction efficiency of furfural by organic solvent and separation-enrichment effect of components. In order to improve the *R* value, metal salts (such as NaCl and $CaCl_2$) can be added to the reaction phase to promote the transfer of furfural from the aqueous phase to the organic phase, thus improving the furfural distribution ratio (Wang 2019). The volume ratio of organic phase to aqueous phase would influence the furfural production. The increase of aqueous content would enhance the rehydration of furfural, resulting in insufficient extraction of furfural to the organic phase. On the other hand, the aqueous phase is the reaction phase, and the decrease of its content could reduce the contact between xylose and the catalyst, thus reducing the furfural yield (Qing et al. 2017). The organic solvent in the biphasic system is generally used as the extraction phase, which should eventually be able to achieve effective separation from furfural, so the boiling point should also be considered. The boiling point of SBP (227 °C) is higher than furfural (162 °C), while the boiling point of other organic solvents is lower than furfural, such as 2-butanol (99 °C), toluene (110 °C), MIBK (117 °C), THF (66 °C), CPME (106 °C), 2-MTHF (80 °C), and DCM (40 °C). Therefore, furfural is distilled out during fractionation in SBP, which is more economically feasible than the case that organic solvent be distilled out in furfural.

**Table 13.4** Classification of biphasic system in furfural production

| Classification | Example | Reference |
|---|---|---|
| $H_2O$/Organic solvent | $H_2O$/SBP | Li et al. (2015b) |
| | $H_2O$/MIBK | Qi et al. (2020) |
| | $H_2O$/2-MTHF | Vomstein et al. (2011) |
| | $H_2O$/THF-MIBK | Morais et al. (2016) |
| MSH/Organic solvent | $LiBr \cdot 3H_2O$/DCM | Yoo et al. (2017) |
| Organic solvent/Organic solvent | NaCl-DMSO/SBP | Li et al. (2015a, b) |
| Co-solution/Organic solvent | NaCl-DMSO-$H_2O$/SBP | Li et al. (2015a) |
| $H_2O$/Supercritical fluid | $H_2O$/supercritical $CO_2$ | Sangarunlert et al. (2007) |
| $H_2O$/Organic solvent-gas | $H_2O$/THF-$CO_2$(q), $H_2O$/THF-$CO_2$(l) | Morais and Bogel-Lukasik (2016) |

## 13.3.3 Catalyst

The selective dissolution and conversion of hemicellulose into furfural need to be carried out under harsh conditions. In the preparation process, the addition of catalyst can significantly accelerate the cleavage of the bond, improving the reaction rate of hemicellulose hydrolysis and pentose dehydration to furfural. Thus, the yield and purity of furfural will be significantly improved. The commonly used catalysts can be divided into homogeneous catalyst and heterogeneous catalyst.

### 13.3.3.1 Homogeneous Catalyst

Homogeneous catalysts refer to catalysts that can be dissolved in reaction systems, including inorganic acids, organic acids, metal salts, and ionic liquids (Table 13.5). Inorganic acids were originally used in furfural production and are still being optimized for furfural production. Sulfuric acid ($H_2SO_4$) and hydrochloric acid (HCl) is often used as catalyst in industry. In recent years, some unconventional inorganic acids such as sulfamic acid ($NH_2SO_3H$), $H_3PW_{12}O_{40}$ have been employed in furfural production, and found to be effective catalysts (Dias et al. 2005a; Zhang et al. 2019b). The advantages of inorganic acid are simple in operation and low in cost, but it has a series of problems such as complex acid recovery process, equipment corrosion, and environmental pollution. Therefore, organic acids such as maleic acid ($C_2H_2(COOH)_2$), acetic acid ($CH_3COOH$), and formic acid (HCOOH) have gradually become research hotspots (Zhang and Zhao 2010; Kim et al. 2012; Yang et al. 2012b). Metal salts such as $SnCl_4$, $AlCl_3$, $FeCl_3$, and $CrCl_2$ are the most used catalysts after HCl and $H_2SO_4$, belong to Lewis acid, which can isomerize D-xylose to D-xylulose and further dehydrated it to furfural (Wang 2015; Delbecq et al. 2018; Nie et al. 2019b). The combination of metal chloride and Brønsted acid can significantly improve the catalytic effect. For example, the addition of $CrCl_2$ in HCl led to a higher selectivity and furfural yield (Binder et al.

**Table 13.5** Classification of homogeneous catalysts in furfural production

| Classification of homogeneous catalysts | Example | Reference |
|---|---|---|
| Inorganic acid | $H_2SO_4$, HCl, $H_3PO_4$, Sulfamic acid ($NH_2SO_3H$) | Lenihan et al. (2010), Avci et al. (2013), Kim et al. (2016), Xiouras et al. (2016), Mazar et al. (2017), Zhang et al. (2019a) |
| Organic acid | Acetic acid, Formic acid, Methanesulfonic acid, Maleic Acid | Kim et al. (2012), Yang et al. (2012b), Delbecq et al. (2018) |
| Metal salt | $AlCl_3$, $FeCl_3$, $CrCl_2$, $SnCl_4$, $NaHSO_4$, $KAl(SO_4)_2$, $Al_2(SO_4)_3$ | Shi et al. (2015), Delbecq et al. (2018), Nie et al. (2019b) |
| Ionic liquid | EMIMCl, [BMIM]$HSO_4$ | Binder et al. (2010a), Carvalho et al. (2015) |
| Sub/supercritical fluid | Subcritical water, High-pressure $CO_2$-$H_2O$ | Toor et al. (2011), Morais et al. (2016) |

2010a). In addition, ILs are green sustainable solvents, some ILs were often applied as acidic catalysts (Lima et al. 2011; Peleteiro et al. 2016a), such as 1-ethyl-3-methylimidazolium chloride (EMIMCl), 1-butyl-3-methylimidazolium hydrogen sulfate ([BMIM]$HSO_4$), 1-ethyl-3-methylimidazolium hydrogen sulfate ([EMIM] $HSO_4$) (Lima et al. 2009; Binder et al. 2010a; Carvalho et al. 2015), etc., but their high cost makes it difficult to realize large-scale industrial production.

At high temperature and pressure, the physical and chemical properties of water will change, such as density, dielectric constant, heat capacity, dynamic viscosity, and ionic product (Toor et al. 2011). Under such conditions, water can ionize hydrogen ions ($H^+$) and hydroxide ($OH^-$), which act as acid or base catalysts to promote the hydrolysis and dehydration reaction of biomass (Akiya and Savage 2002). Catalytic water includes subcritical water (100 °C $>$ $T >$ 374 °C, pressure is enough to keep water in liquid state) and supercritical water ($T >$ 374 °C, $P >$ 218 atm) (Aida et al. 2010; Toor et al. 2011). Hemicellulose readily dissolves and hydrolyzes at temperatures above ~180 °C, and the hydrolysis is both acid catalyzed and base catalyzed (Bobleter 1994). The processes with liquid water under high temperature and pressure are also called autohydrolysis, hydrothermal treatment, hot compressed water, hydrothermolysis, liquid hot water, aquasolve process, aqueous processing and pressure-cooking in water (Ruiz et al. 2013). One upgrade of hydrothermal progress is high-pressure $CO_2$–$H_2O$ method. In recent years, high-pressure $CO_2$–$H_2O$ has been widely used in biomass processing. The in situ formation of carbonic acid acted as catalyst and led to high dissolution of hemicellulose from biomass into xylo-oligosaccharides, xylose, arabinose, and furfural (Silva et al. 2014; Morais et al. 2014, 2016). After reaction, $CO_2$ is easy to recover and recycle in the reaction medium through depressurization step, so the high-pressure $CO_2$-based method is considered as a promising alternative technology in the field of biorefinery. However, the conditions of high temperature and high pressure place high requirements on equipment, making commercialization very difficult.

#### 13.3.3.2 Heterogenous Catalyst

Heterogeneous catalyst refers to the catalyst which is immiscible with the reaction system. Compared with homogeneous catalyst, heterogeneous catalyst is a kind of reusable catalyst, which solves the problems of separation and recycling. It has been widely studied, including metal oxide, zeolite molecular sieves (ZMS), metal salts, heteropoly acid, natural clay minerals, ion-exchange resins, and so on (Bhaumik and Dhepe 2014; Li 2016). Heterogeneous catalyst gradually replaces liquid acid catalyst because of its advantages such as low corrosion, safety, green, and easy separation. Heterogeneous acid catalyst refers to the solid that can provide proton (Brønsted acid) or receive electron pair (Lewis acid). The acid sites on the surface of heterogeneous with catalytic activity are called acid sites, namely Brønsted acid center and Lewis acid center (Tong et al. 2010). In the process of biomass conversion to furan chemicals, Lewis acid is conducive to hydrolysis and isomerization, while Brønsted acid is conducive to dehydration. Therefore, when both Lewis acid and Brønsted acid are present on the catalyst surface, xylose can be effectively isomerized to xylulose, which is then dehydrated to furfural. Heterogeneous catalysts are classified

**Table 13.6** Classification of heterogeneous acid catalysts

| Classification | | Example | Reference |
|---|---|---|---|
| Low porosity catalyst | Ion-exchange resin | Nafions and Amberlysts: Nafion 117, Amberlyst-15 | Agirrezabal-Telleria et al. (2014), Yan et al. (2014) |
| Microporous acid catalyst | Zeolite (aluminosilicate) | Faujasite, mordenite, delaminated zeolite | Moreau et al. (1998), Lima et al. (2008) |
| | Zeolite-type silicoaluminophosphate (SAPO) | SAPO-5, SAPO-11 | Lima et al. (2010) |
| Mesoporous acid catalyst | Metal oxide | Mono-Oxide: $Al_2O_3$, $ZrO_2$, $TiO_2$ | Weingarten et al. (2011) |
| | | Multiple oxide: $Al_2O_3$-$SiO_2$, $Al_2O_3$-$ZrO_2$, $SO_4^{2-}$/$TiO_2$-$ZrO_2$/$La^{3+}$ | Li et al. (2014a), Li et al. (2014b), You et al. (2014) |
| | Metal phosphate | $NbOPO_4$, $TaOPO_4$ | Delbecq et al. (2018) |
| | Silicate | Mesoporous: MCM-41, SBA-15; Microporous: AM-11 | Dias et al. (2005a) |
| | | Modified: Coated MCM-41-$SO_3H$; MCM-Nb16 | Dias et al. (2005b), García-Sancho et al. (2013) |
| Supported Catalyst | Acid sites/support | $H_3PW_{12}O_{40}$/MCM-41, $SO_4^{2-}$/Sn-MMT, ILs/$SiO_2$ | Dias et al. (2006b), Lin et al. (2017), Xu et al. (2015) |

in various ways (Lima et al. 2010; Karinen et al. 2011; Delbecq et al. 2018). According to their pore structure characteristics, heterogeneous catalyst can be divided into low porosity catalyst, microporous and mesoporous acid catalyst. Microporous/mesoporous acid catalysts can also be used as support materials, for example, the strongly acidic 12-tungstophosporic acid (PW) can be supported on mesoporous silica MCM-41. The commonly used heterogeneous catalysts are shown in Table 13.6.

In addition, microporous sulfonic acid, layered niobate titanate, layered aluminosilicate, Tungstophosphate, nafion117, and zirconia are also commonly used solid catalysts in the preparation of furfural (Yan et al. 2014). With the popularity of biomass refining concept, the preparation of furfural with biomass-based solid catalyst has gradually attracted people's attention. In general, the application of solid catalyst in furfural production process has great development potential. In the process of reaction, carbon deposition (such as humins formation) will reduce the surface active sites of the catalyst and greatly reduce the catalytic activity, so it is necessary to use special methods to regenerate the catalyst. Therefore, the stability and recycling performance of solid catalysts are the focus of researchers.

### 13.3.4 Temperature, Time, Heating Method and Additive

Reaction temperature and duration time are two important factors affecting the dehydration reaction of xylose. In the process of furfural production, the temperature is generally 150–200 °C and the time is from a few seconds to several hours. The activation energy barrier of dehydration of xylose to furfural is high (124 kJ/mol) (Choudhary et al. 2011), so low temperature ($<150$ °C) is not powerful enough for xylose to cross the reaction barrier to obtain furfural. In the sealed reactor (without the replenishment of reactant and transpiration of product), when increase the temperature and prolong the reaction time, furfural yield would decline after reaching the maximum value. This is due to the side reaction of furfural, including fragmentation and condensation reactions which form soluble degradation products and black insoluble solids (humins) (Antal et al. 1991; Li 2001; Karinen et al. 2011). Therefore, suitable temperature and time are important factors for obtaining high furfural yield.

Microwave-assisted heating has increased over the last years to become very popular in the world because of its many advantages, such as the shorter reaction time, uniform heating and higher reaction efficiency. It has been shown that microwave-assisted heating has yielded more furfural compared to traditional heating methods (Guenic et al. 2015). However, microwave-assisted heating has disadvantages, including high energy consumption, small scale, and low universality, which make it impossible for industrial application in a short time (Calcio et al. 2019).

Different additives such as thiourea, $NaHSO_4$, NaCl, KBr, betaine chloride were addition during furfural production with role of co-catalyst, promoter, or phase modifier (Delbecq et al. 2016, 2018; Yazdizadeh et al. 2016; Qing et al. 2017; Xu et al. 2017). The liquid–liquid equilibrium (LLE) of systems would be altered in the presence of dissolved salts. This phenomenon is termed “salting-out” which leads to an increase in the distribution coefficient of an extractable species from aqueous phase in the presence of a salt (Saien and Norouzi 2011). NaCl was selected as a phase modifier in the biphasic system due to its low price and accessibility (Qing et al. 2017). Generally, the addition of NaCl led to the increase of furfural yield, xylose conversion, and furfural selectivity. Furthermore, it was believe that $Cl^-$ ions acted as a catalyst during the conversion of xylose to furfural (Guenic et al. 2015). Marcotullio and Jong (2010) suggested that $Cl^-$ ions promoted the formation of the 1,2-enediol from the acyclic form of xylose and thus the subsequent acid catalyzed dehydration to furfural. Luo et al. (2017) found that $Cl^-$ formed hydrogen bonds with α-, β-OH-2,3,4 of the xylose unit in DMSO-$d_6$, thus promoting the cleavage of C1–O6 and dehydration of xylose to form furfural. Xu et al. (2017) investigated the furfural production from the conversion of corncob using sulfuric acid as catalyst and thiourea as additive. A higher furfural yield was achieved using thiourea as additive compared with that without additive. The reaction kinetic of furfural degradation shows that the activation energy is increased by 21% with thiourea as additive, which confirms that thiourea has effect on inhibiting the furfural degradation.

## 13.4 Furfural Production

### 13.4.1 Production of Furfural from Xylose

Xylose is the main monosaccharide of xylan-type hemicellulose in lignocellulosic biomass. One of the key steps in the production of furfural from biomass is the dehydration reaction of the xylose. Therefore, xylose is used as the model compound to study effective strategies to improve furfural yield and explore feasible paths suitable for industrial furfural by many researchers (Table 13.7).

Inorganic acids (such as HCl and $H_2SO_4$) are the most used catalysts in the industrial furfural production processes, which have been studied for many decades. The selectivity of furfural in the process of using single inorganic acids is generally

**Table 13.7** The conversion of xylose to furfural

| Solvent | Catalyst | Conditions | Yield (%)[a] | Reference |
|---|---|---|---|---|
| NaCl-$H_2O$ | HCl | 200 °C, 5 min | 81 | Marcotullio and Jong (2010) |
| GVL-$H_2O$ | $H_2SO_4$ | 170 °C, 15 min | >80 | Gürbüz et al. (2013) |
| GVL-$H_2O$ | H-Mordenite | 175 °C, 120 min | 80 | Gürbüz et al. (2013) |
| GVL | $H_2SO_4$ | 175 °C, 15 min | 75 | Gallo et al. (2013) |
| $H_2O$ | $FeCl_3$ | 170 °C, 20 min | 69 | Guenic et al. (2015) |
| SBP/NaCl-DMSO | Sn-MMT | 180 °C, 30 min | 77 | Li et al. (2015b) |
| [BMIM][$HSO_4$] | – | 140 °C, 90 min | 37 | Peleteiro et al. (2015) |
| [BMIM][$HSO_4$]/toluene | – | 140 °C, 240 min | 74 | Peleteiro et al. (2015) |
| [BMIM][$HSO_4$]/MIBK | – | 140 °C, 300 min | 80 | Peleteiro et al. (2015) |
| [BMIM][$HSO_4$]/dioxane | – | 140 °C, 240 min | 82 | Peleteiro et al. (2015) |
| NaCl-$H_2O$ | HCl | 200 °C, 10 min | 64 | Vaz and Donate (2015) |
| NaCl-$H_2O$ | $NiCl_2$ | 200 °C, 10 min | 50 | Vaz and Donate (2015) |
| GVL-$H_2O$ | $NH_2SO_3H$ | 190 °C, 15 min | 70 | Zhang et al. (2019b) |
| $H_2O$/DCM | Carbon-based solid acid | 180 °C, 90 min | 98 | Lin (2020) |
| GBL-$H_2O$ | – | 180 °C, 2.5 h | 46 | Lin et al. (2020) |

[a]The yield of furfural was based on the moles of pentosan in biomass

low, so in the last decade, researchers proposed the method of adding additives or change the heating way to improve the efficiency of furfural production.

Marcotullio and Jong (2010) obtained 81% yield and 90% selectivity of furfural using xylose as the starting material in 50 mM HCl solution containing 850 mM NaCl under heating at 200 °C for 5 min. It was found that the furfural yield was 20% higher than that without NaCl, which indicated that the $Cl^-$ as catalyst promote the formation of the 1,2-enediol from the acyclic form of xylose, and thus the subsequent acid catalyzed dehydration to furfural.

The novel alternative technology, microwave heating, was developed to produce furfural from xylose. Vaz and Donate (2015) applied microwave as a green synthetic methodology to convert xylose into furfural. The highest yields of furfural were obtained at the HCl concentration of 4 mg/mL. When the reaction was performed at 200 °C, an optimum yield of 64% of furfural was observed after 10 min of reaction time, with 95% of the xylose being converted.

Except traditional inorganic acids, some new kind of inorganic acids have been employed in the last decade. Zhang et al. (2019b) obtained a high yield (70%) of furfural in GVL/water at 190 °C for 15 min from xylose using sulfamic acid ($NH_2SO_3H$) as catalyst. The potential catalytic mechanism of sulfamic acid was also studied. It is hypothesized that the zwitterionic unit ($H_3N^+SO^{3-}$) is crucial in efficiently catalyzing isomerization reaction, leading to the xylose tautomerization to xylulose, a shorter route to furfural, and finally, the $NH_2SO_3H$ with strong acidity also promotes the xylulose dehydration to furfural.

Compared with inorganic acids, organic acids such as formic acid and acetic acid are less corrosive and easy to be separated and recovered, which can be used as catalyst for furfural production. Yang et al. (2012b) reported that formic acid has higher furfural yield and selectivity than phosphoric acid and sulfuric acid. The highest 78% selectivity of furfural was obtained from the conversion of xylose with the initial condition of 40 g/L xylose and 10 g/L formic acid at 180 °C.

Some metal salts with Lewis acid sites have strong catalytic activity for furfural formation, such as metal chlorides, metal sulfates, and metal bromides. Compared with inorganic acids, metal chlorides have low corrosivity, recyclability, and high catalytic efficiency. Guenic et al. (2015) studied the effect of different metal chlorides ($CuCl_2$, $CoCl_2$, $ZnCl_2$, $FeCl_2$, $FeCl_3$, $AlCl_3$, $CrCl_3$) and iron sulfates ($FeSO_4$, $Fe_2(SO_4)_3$) on the dehydration of xylose at 170 °C for 20 min. $FeCl_3$ resulted in the highest furfural yield (69%) during these catalysts. It was found that $Fe^{3+}$ gave better furfural yields than those obtained in presence of $Fe^{2+}$, and the anion $SO_4{}^{2-}$ was less effective than $Cl^-$ in favoring the conversion of xylose. Vaz and Donate (2015) studied the influence of the addition of chlorides and bromides ($CuCl_2$, $CaCl_2$, $NiCl_2$, $MgCl_2$, $ZnBr_2$, $MgBr_2$, $CuBr_2$, $FeCl_3$) on the furfural production. The highest furfural yield (50%) was achieved by using $NiCl_2$ as catalyst when comparing to other catalysts.

The acidic ionic liquids can be a reaction medium or/and a catalyst in the furfural production from xylose. Peleteiro et al. (2015) dissolved xylose in [BMIM][$HSO_4$] in the absence of externally added catalysts. 37% of furfural yield was achieved in single [BMIM][$HSO_4$] phase, while the furfural yields were improved to 74%, 80%, and 82% in the presence of toluene, methyl isobutyl ketone or dioxane as extraction solvents, respectively, in which [BMIM][$HSO_4$] acted as both a medium and a catalyst.

Heterogeneous catalyst, especially solid acid, can solve the problem of catalyst recovery, so it has attracted much attention in the production of furfural. $SO_4^{2-}/M_xO_y$ solid acid catalyst has been used in the furfural production due to its high acidity and stability. The maximum furfural yield from xylose conversion reached 43% using solid superacid $SO_4^{2-}/TiO_2$, while under the same conditions the yield of furfural was only 16% with $H_2SO_4$ as catalyst (Wu and Sun 2012). $SO_4^{2-}/M_xO_y$ solid acid catalyst also exhibited many advantages, such as short life and sensitivity to synthesis conditions. Therefore, it is of great significance to study the optimal composition and preparation conditions of composite metal oxides to improve their catalytic activity and selectivity. Zhang et al. (2011) obtained 54% yield of furfural using $SO_4^{2-}/ZrO_2\text{-}TiO_2$ catalyst at 190 °C for 4 h. On this basis, Li et al. (2014a, b) developed $SO_4^{2-}/TiO_2\text{-}ZrO_2/La^{3+}$ solid acid catalyst for xylose conversion. At 180 °C for 12 h, the maximum furfural yield reached 3563.3 μmol/g (based on the weight of xylose) in a two-phase system ($H_2O$:DMI/MIBK:2-Butanol, 8:2/7:3).

Molecular sieve (MS) solid acid catalyst is a kind of acid material mainly composed of crystalline silicate and aluminate, which is widely used in furfural production. Kaiprommarat et al. (2016) used sulfonated MS $SO_3H$-MCM-41 to catalyze xylose to furfural and found that the acid strength of the catalyst greatly affected the conversion of xylose, and there was a certain relationship between the pore structure of the catalyst and furfural selectivity. When the catalyst has wormhole structure and pore size is between 3 and 6 nm, the furfural selectivity can reach 93–98%, and the furfural yield can reach 69% at 155 °C for 2 h. MS possesses significant advantages such as larger specific surface area, better adsorption capacity, and product shape selection ability than solid mixed metal-oxide catalysts, but it also has the disadvantages of small size, less available active sites on the surface and low thermal stability. Therefore, improving the thermal stability of MS is crucial to realize its efficient utilization.

Carbon-based solid acid catalyst is sulfonated carbon material, which is a new heterogeneous catalyst with simple preparation and low cost. Its preparation method is that organic material such as biomass was first partially carbonized under high temperature and oxygen isolation. Carbon-based solid acids have high thermal stability due to incomplete carbonization, and are insoluble in water and organic solvents. After sulfonation, they contain a large number of acid groups such as –COOH, –$SO_3H$, and phenolic –OH groups (Deng 2016). Carbon-based solid acid catalysts have attracted much attention in recent years in furfural preparation. Zhang et al. (2016) prepared SC-CCA by using *p*-diazobenzenesulfonic acid instead of concentrated $H_2SO_4$ to sulfonate the carbonized carbon-based materials. The yield of furfural reached 79% from xylose conversion with SC-CCA as catalyst in GVL at 170 °C for 30 min, and the performance of the catalyst was not significantly reduced after five reuses. Khatri et al. (2015) prepared P-C-$SO_3H$ catalyst, which was obtained by sulfonation of carbonized glucose. The maximum furfural yield from xylose was 89% using this catalyst in DMSO solution. Lin (2020) prepared C600-S carbon-based catalyst by carbonization and sulfonation of industrial furfural residue. This catalyst was used to catalyze xylose in DCM/$H_2O$ system at 180 °C for 90 min, and nearly 100% xylose conversion and 98% furfural yield were obtained. In the work of Qi et al. (2020), the conversion of xylose to furfural was effectively achieved in a $H_2O$/MIBK biphasic system catalyzed by synthesized magnetic carbon-based solid acid catalyst, and the highest furfural yield of 79% was obtained at 190 °C for 10 min.

Green solvent such as water, γ-valerolactone (GVL), 2-methyltetrahydrofuran (2-MTHF) is expected to replace petroleum-derived solvent for the conversion of xylose. Among these solvents, GVL was considered as a biomass-derived green solvent and it was identified as an effective solvent in furfural preparation compared to $H_2O$ (Luo et al. 2019). Some researchers tested the effect of a variety of polar aprotic organic solvents on the catalytic conversion of xylose to furfural by reaction kinetics and found that the reaction rate and product selectivity were significantly improved using GVL as solvent, their results showed that the use of GVL as the solvent changed the activation energies for the dehydration of xylose to furfural. Mellmer et al. (2014) determined that the apparent activation energies for furfural formation from xylose and furfural degradation in $H_2O$ were 145 kJ/mol and 85 kJ/mol, respectively, which are consistent with reported values (Williams and Dunlop 1948). When GVL was used as solvent, the activation energy barrier for xylose dehydration decreased to 114 kJ/mol, whereas the barrier for furfural degradation increased to 105 kJ/mol, which was conducive to the formation of the desired furfural product. Gallo et al. (2013) studied the dehydration reaction of xylose in GVL and found that reactions occurred faster and degradation products were less than in water. The yield of furfural was about 75% under the catalysis of $H_2SO_4$ at 175 °C for 15 min. It was also found that the furfural yield was more than 80% when 10 wt% water was added into the solvent of GVL under similar conditions, which confirmed that the conversion of xylose to furfural could be further improved by using GVL-$H_2O$ co-solvent system (Gürbüz et al. 2013). Water is the cheapest green solvent, but the side reactions of furfural in the water phase result in a low yield. Therefore, some co-solvents such as γ-butyrolactone (GBL), dimethyl sulfoxide (DMSO), and GVL have been developed to inhibit the side reactions of furfural. Lin et al. (2020) obtained 34% furfural from the hydrothermal reaction of xylose at 180 °C for 2.5 h in the water (without catalyst), however, the furfural yield reached 46% in GBL-$H_2O$ system (volume ratio 1:1) under the same conditions. Through molecular dynamics simulation by Gromacs software, it was found that GBL has a weaker affinity with xyose than DMSO, *N*,*N*-dimethylformamide (DMF), and isopropanol, but has a stronger affinity with furfural. Therefore, GBL can provide furfural protective shell and play a positive role in furfural production. In the GBL-$H_2O$ system (without catalyst), there is a micro two-phase region, in which xylose is surrounded by water and furfural is surrounded by GBL, effectively inhibiting the degradation of furfural.

The biphasic system can significantly inhibit the side reaction of furfural, and there are many biphasic systems for xylose conversion, such as methyl isobutyl ketone (MIBK)/$H_2O$, 2-sec-butylphenol (SBP)/NaCl-DMSO, dichloromethane

(DCM)/$H_2O$, toluene/$H_2O$, cyclopentyl methyl ether (CPME)/$H_2O$, 2-methyltetrahydrofuran (2-MTHF)/$H_2O$, 2-butanol/$H_2O$, and tetrahydrofuran (THF)/$H_2O$. Li et al. (2015b) used Sn-MMT as a solid acid catalyst for the heterogeneous catalytic transformation of xylose. At 180 °C for 30 min, the highest furfural yields were reached 77% from xylose with 93% xylose conversion and 82% furfural selectivity in SBP/NaCl-DMSO biphasic system. A DCM/$H_2O$ system was developed to inhibit the oxidation of furfural (Deng et al. 2016a; Cheng et al. 2018; Lin 2020). In this system, Lin (2020) used carbon-based catalysts loaded with sulfonate as catalyst, and obtained 98% furfural yield with nearly 100% xylose conversion at 180 °C for 90 min. This indicated that the condensation reaction between furfural and xylose was prevented by the extraction of furfural from aqueous phase to organic phase by DCM. In the $H_2O$/DCM system, the density of DCM is higher than that of water, so the furfural formed by xylose dehydration is extracted by DCM and exists in the bottom layer of the system, which effectively inhibits the oxidation reaction of furfural in contact with oxygen, thus improving the yield of furfural.

### 13.4.2 Production of Furfural from Hemicellulose

Excepting xylose as model compounds to produce furfural, many researchers use xylan-type hemicellulose as starting materials in the production of furfural (Table 13.8). The furfural production from xylan is more complex than that from xylose, which requires both hydrolysis and dehydration. Xylan is first hydrolyzed to xylose, which is subsequently dehydrated to furfural. Similar to the production of

**Table 13.8** The conversion of xylan to furfural

| Solvent | Catalyst | Conditions | Yield (%)[a] | Reference |
|---|---|---|---|---|
| $H_2O$ | HCl | 180 °C, 30 min | 36[b] | Yemi and Mazza (2011) |
| THF/$H_2O$ | $AlCl_3 \cdot 6H_2O$-NaCl | 140 °C, 45 min | 64 | Yang et al. (2012c) |
| GVL-$H_2O$ | $FeCl_3 \cdot 6H_2O$ | 170 °C, 35 min | 67 | Zhang et al. (2014) |
| 2-MTHF/$H_2O$ | $SnCl_4$ | 150 °C, 120 min | 78 | Wang et al. (2015) |
| GVL-$H_2O$ | $Al_2(SO_4)_3$ | 130 °C, 30 min | 88 | Yang et al. (2017) |
| 2-MTHF/NaCl-$H_2O$ | $SO_4^{2-}$/Sn-MMT | 160 °C, 90 min | 77 | Lin et al. (2017) |
| MIBK/$H_2O$ | HCl | 177 °C, 60 min | 46 | Sweygers et al. (2018) |

[a] The yield of furfural was based on the moles of pentosan in biomass

[b] The yield of furfural was based on the weight of pentosan in biomass

furfural from xylose, the promoted methods including process intensification, catalyst design, solvent system are applied during the conversion of xylan to furfural.

Microwave can significantly accelerate the reaction rate of furfural formation from xylan. Yemi and Mazza (2011) investigated the acid catalyzed conversion of xylan to furfural by microwave-assisted reaction at ranges of temperatures and time (140–190 °C, 1–30 min), and obtained highest 36 wt% furfural yield using 0.1 M HCl at 180 °C for 30 min.

Some organic solvents (e.g. GVL, THF, 2-MTHF) and homogeneous catalysts with Lewis acidity (e.g. $FeCl_3 \cdot 6H_2O$, $SnCl_4$, $AlCl_3 \cdot 6H_2O$, $Al_2(SO_4)_3$) was widely used in the conversion of xylan to furfural. Wang et al. (2015) studied the catalytic transformation of xylan with $SnCl_4$ as catalyst in bio-based 2-MTHF/$H_2O$ biphasic system, and obtained 78% yield of furfural at 150 °C for 120 min. Yang et al. (2017) studied the conversion of xylan to furfural using $Al_2(SO_4)_3$ catalyst in GVL/$H_2O$ solvent system, and 88% furfural was obtained under microwave heating at 130 °C for 30 min. The biphasic system has also been used in the furfural production from xylan. Lin et al. (2017) prepared $SO_4^{2-}$/Sn-MMT catalyst for the heterogeneous catalytic conversion of xylan. At 160 °C for 90 min, the highest furfural yields were reached 77% from xylan in 2-MTHF/NaCl-$H_2O$ biphasic system.

Li et al. (2016) studied the effect of alkali-soluble corncob hemicelluloses structure on the furfural production. It was found that the alkali-soluble corncob hemicelluloses with lower branch degree, higher xylose content, higher polydispersity and crystallinity is facilitate to the furfural production. The authors used tin-loaded montmorillonite (Sn-MMT) as a catalyst, 2-sec-butylphenol (SBP)/NaCl-DMSO as solvent system, obtaining 45% furfural yield from the oven-dried hemicelluloses precipitated at the 30% (v/v) ethanol.

### 13.4.3 "One-Pot" Method for Furfural Production from Lignocellulosic Biomass

A series of studies on the conversion of xylose and pure hemicellulose to furfural are valuable to understand the formation mechanism of furfural, which opened the possibility of using more complex carbohydrate, such as raw biomass, as a starting material. Furthermore, the use of xylose and pure hemicellulose as a substrate in the production of furfural was not an economically viable option, as they needed to be separated from biomass and the structures of hemicellulose are not the same as those of the actual hemicellulose in actual biomass. Therefore, the production of furfural from hemicellulose in actual biomass was more challenging but feasible than from xylose and pure hemicellulose.

Due to the complicated interactions of the three main components in biomass, the dissolution of hemicellulose in one-pot method is always accompanied with the partial dissolution of cellulose and lignin. Industrially, the conventional one-pot method used homogeneous mineral acid catalysts ($H_2SO_4$) to catalyze xylan-type hemicellulose of lignocellulosic biomass in aqueous solutions and only 40–50% furfural was obtained. Therefore, it is necessary to develop more economic and environmentally strategies for furfural production from hemicellulose in biomass. In recent years, a new biorefinery model based on multi-product has been developed. It improves the "one-pot" process of the traditional furfural industry, realizes the efficient utilization of the three major components of biomass, and achieves the goal of multi-product co-production. Up to this day, "one-pot" methods including selective dissolution and conversion of hemicellulose in raw biomass to furfural, the simultaneous conversion of hemicellulose and lignin, the simultaneous conversion of hemicellulose and cellulose and simultaneous conversion of all the three main components firstly and then recovered one dissolved component.

The "one-pot" method to produce furfural from the selective dissolution and conversion of hemicellulose in raw biomass has been extensively studied. Homogeneous metal chloride catalyst has attracted much attention due to its ability to promote the selective conversion of hemicellulose to furfural. Yang et al. (2012c) investigated the selective dissolution of hemicellulose in NaCl-THF/$H_2O$ systems promoted by $AlCl_3$. The furfural yield of 55%, 38%, 56%, and 64% were obtained, respectively, from corn stover, pinewood, switch grass, and poplar at 160 °C for 45 min. The aqueous phase containing $AlCl_3 \cdot 6H_2O$ and NaCl remained the activity and selectivity for furfural during five cycles.

In order to further improve the selectivity of hemicellulose to furfural, the design of solid acid has been explored to realize the efficient dissolution of hemicellulose from the cell wall, leaving a rather pure cellulose and lignin as solid residue. Wang et al. (2018) realized high selective dissolution and conversion of hemicellulose from unground bagasse using $SO_4^{2-}$/Sn-MMT as catalyst, and 88% furfural yield was obtained in SBP/NaCl-DMSO-$H_2O$ biphasic system by hydrothermal treatment. The cellulose fraction in residue continued to react in this system to produce levulinic acid (62%), leaving a mixture of lignin and solid acid catalyst, which can be separated by sieving. Bhaumik and Dhepe (2014) proposed a highly efficient one-pot pathway for the selective conversions of hemicelluloses from raw biomass (bagasse, rice husk and wheat straw). Furfural with a high yield (86–93%) was obtained at 170 °C for 8 h in $H_2O$/toluene (1:2) biphasic solvent system using silicoaluminophosphate, namely SAPO-44, as catalysts. A one-step process was proposed for valorization of corn stover into furfural catalyzed by SAPO-18 zeolites by Li et al. (2019). At the fixed catalyst concentration of 20 g/L, a furfural yield of 95.1% was observed at 205 °C for 40 min using SAPO-18 with Brønsted to Lewis acid site ratio of 0.11. The SAPO-18 with lower Brønsted to Lewis acid site ratios showed higher activity for furfural production from corn stover. Li et al. (2020) developed a clean and efficient catalytic system consisting of sulfonated carbon microspheres catalysts and γ-valerolactone for the upgrading of waste lignocellulose to the furfural in one-pot. The highest furfural yields for corncob, corn straw, and Eucalyptus sawdust were 74%, 70%, and 72%, at 170 °C for 120 min, 170 °C for 60 min, and 170 °C for 120 min, respectively. Zhang et al. (2018) employed *p*-hydroxybenzenesulfonic acid-formaldehyde resin acid catalyst (MSPFR) for the furfural production from raw corn stover. A high furfural yield of 50% was obtained at 190 °C for 100 min when the MSPFR/corn stover mass loading ratio was 1 with GVL as solvent. Zhang et al. (2019a) prepared a bifunctional carbonaceous solid acid (with functional groups of –COOH, phenolic –OH, –Cl, and $–SO_3H$) to employ in the production of furfural from corncob, in which a furfural yield of 91% was achieved at 448 K in 30 min in γ-valerolactone/water system.

Hemicellulose and lignin were also converted simultaneously in the one-pot treatment of lignocellulosic biomass. Luo et al. (2017) developed a GVL-$H_2O$ co-solvent system for the simultaneous conversion of hemicellulose and lignin from pubescens. 34 wt% yield of furfural was obtained (based on the weight of C5 fraction in pubescens), accompanied with a lower molecular weight lignin derivatives (150–500 Da) at 160 °C for 4 h. The authors also found that $H_2O$ promoted the cleavage of chemical bonds linking hemicellulose, lignin, and cellulose, and GVL further helped the co-dissolution of hemicellulose (94 wt%) and lignin (80 wt%), leaving a high purity cellulose (83 wt%).

In addition, the simultaneous dissolution and conversion of carbohydrates also existed in the one-pot treatment. Molten salt hydrate (MSH), a high concentration inorganic salt solution, can be used as a solvent and reaction medium for biomass conversion. Some MSHs, such as $LiBr \cdot 3H_2O$, $ZnCl_2 \cdot 4H_2O$, were used to dissolve carbohydrates. Yoo et al. (2017) used lithium bromide hydrate solution ($LiBr \cdot 3H_2O$) for the simultaneous conversion of carbohydrates in real biomass (herbage, hardwood, and softwood). At 125 °C for 2 h, the yields of furfural and bromomethylfurfural (BMF) from hemicellulose and cellulose were about 70% and 85%, respectively, in $LiBr \cdot 3H_2O$/DCM biphasic system using HBr as catalyst. However, lignin in the biomass was significantly depolymerized and separated with high purity for potential coproducts.

In some one-pot treatment, simultaneous dissolution of all the three main components firstly also occurs, then one component was recovered by special means. Alonso et al. (2013) reported a process for the simultaneous dissolution of all the three main components of corn stover. The mixture of hemicellulose and cellulose was obtained in 90% GVL-$H_2O$ solvent using 0.025 M $H_2SO_4$, 96% furfural and 10% levulinic acid (LA) can be achieved, respectively, from the conversion of hemicellulose and cellulose at 443 K for 0.5 h, while under the same conditions for 4 h, the yields of furfural and levulinic acid were 73% and 51%. The dissolved lignin was precipitated upon addition of water and removed by filtration. Compared with GVL solvent, the utilization of a lower boiling point solvent, THF, also achieved the simultaneous hydrolysis of carbohydrates in lignocellulosic biomass. Li et al. (2014c) studied the integrated conversion of three main components of bagasse in THF/$H_2O$ (2:1) biphasic system. The yield of furfural and levulinic acid were 66% and 44%, respectively, under 0.4 M HCl treatment at 200 °C for 30 min. Their work realizes the simultaneous conversion of cellulose and hemicellulose, while lignin was dissolved first and then precipitated as a solid residue.

Although high yields of furfural are obtained in the one-pot process, the selectivity to furfural is still low because of the undesirable products produced by side reactions. For example, cellulose is converted to furan compounds, levulinic acid or formic acid, and lignin is partially converted to phenolic compounds when reaction conditions are harsh. The products obtained from the conversion of hemicellulose,

**Table 13.9** "One-pot" method for the preparation of furfural from lignocellulosic biomass

| Feedstock | Solvent | Catalyst | Conditions | Yield (%)[a] | Reference |
|---|---|---|---|---|---|
| Bagasse | SBP/NaCl-DMSO-$H_2O$ | $SO_4^{2-}$/Sn-MMT | 170 °C, 2.4 h | 88 | Wang et al. (2018) |
| Bagasse | $H_2O$/*p*-xylene | HUSY | 170 °C, 6 h | 56 | Sahu and Dhepe (2012) |
| Corn stover | GVL-$H_2O$ | 0.025 M $H_2SO_4$ | 170 °C, 30 min | 96[b] | Alonso et al. (2013) |
| Bagasse | $H_2O$/toluene | SAPO-44 | 170 °C, 8 h | 93 | Bhaumik and Dhepe (2014) |
| Bagasse | THF/$H_2O$ | 0.4 M HCl, NaCl | 200 °C, 20 min | 66 | Li et al. (2014c) |
| Corn stover | GVL-SBP | 0.05 wt% $H_2SO_4$, $AlCl_3$ | 170 °C, 20 min | 70[b] | Luterbacher et al. (2014) |
| Corncob | $H_2O$ | 0.9 mM $H_2SO_4$ | 160 °C, 1.5 h | 71 | Wang et al. (2014b) |
| Corn stover | GVL-$H_2O$ | SAPO-18 | 205 °C, 40 min | 95.1 | Li et al. (2019) |
| Corn stover | GVL | SC-$CaC_t$-700 | 200 °C, 100 min | 93 | Li et al. (2017a) |
| Pubescens | GVL-$H_2O$ | – | 160 °C, 4 h | 34[b] | Luo et al. (2017) |
| Corncob | GVL | SPTPA | 175 °C, 30 min | 74 | Zhang et al. (2017) |

[a] The yield of furfural was based on the moles of pentosan in biomass

[b] The yield of furfural was based on the weight of pentosan in biomass

cellulose and lignin are mixed together, which is not conducive to the separation and purification of furfural (Table 13.9).

### 13.4.4 Two-Step Method for Furfural Production from Lignocellulosic Biomass

Two-step methods for the conversion of hemicellulose in lignocellulosic biomass included the selective dissolution of hemicellulose from other two components and then further conversion of the hydrolysate (oligomers or xylose) to yield furfural. The two-step procedure was carried out separately. The temperature required in the first step is lower, so the residue after hydrolysis retains the basic structure of cellulose and lignin, which is beneficial to the further utilization of downstream products. Furfural prepared by hydrolysate (mainly from hemicellulose) has the advantages of less by-products and higher yield. Therefore, two-step methods have been proposed as one of the efficient approaches to obtain furfural with high yield and selectivity (Fig. 13.4).

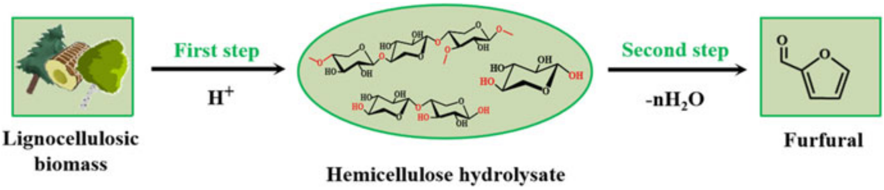


**Fig. 13.4** Two-step method for furfural production from lignocellulosic biomass. The Fig adapted from figure proposed by Ref. (Luo et al. 2019)

To obtain furfural with high yield and selectivity, some measures used in two-step method are as follows (Luo et al. 2019): (1) In the first step, adding homogeneous catalyst, especially replacing minerals acid by organic acids, solid acids and metal chlorides, is conducive to the dissolution and hydrolysis of hemicellulose. In contrast with mineral acid, it was desirable for the development of nonmineral acid with high selectivity and low acidity to hemicellulose to avoid problems such as by-products formation, equipment corrosion, and environmental pollution. A nanoscale (30–50nm) solid acid $SO_4^{2-}/Fe_2O_3$ catalyst was prepared to effectively hydrolyze hemicellulose from wheat straw (Zhong et al. 2015). A maximum hemicellulose hydrolysis yield of 63% could be obtained, while keeping cellulose and lignin inactive. Among organic acid pretreatment, oxalic acid pretreatment is an effective method to separate hemicellulose because of its advantages such as good hydrolysis selectivity, high hemicellulose removal rate, short prehydrolysis time, and low temperature. Deng et al. (2016b) developed a feasible approach for the production of xylose and xylooligomer from corncob. The maximum yield of xylo-sugars was 86% under ball milling for 60 min with 15 mM oxalic acid and followed by the hydrothermal treatment at 130 °C for 30 min. (2) In the second step, adding organic solvent to form a biphasic system, furfural was continuous extracted into the organic phase to inhibit the side reactions, which improved the selectivity and yield of furfural; adding NaCl in the reaction phase to improve the conversion of xylose to furfural by the salt effect; using recyclable solid acid catalysts to promote the depolymerization of hemicellulose derivatives to furfural.

Wang et al. (2019) developed a novel approach to produce furfural with high yield from biomass via two reaction stages. In the first step at the reasonably mild temperature of 140 °C for 120 min, the efficient conversion of hemicellulose in bagasse to xylose with high yields (83%) was achieved in an aqueous solution containing 0.15 M oxalic acid, leaving cellulose and lignin mostly intact (the glucose yield in hydrolysate <5%). The second step was performed at 190 °C for 120 min in a 2-MTHF/$H_2O$-NaCl biphasic system, high yield of furfural (89%) was obtained by the further reaction of xylose hydrolysate using recyclable ironic phosphates ($FePO_4$) catalysts. It was demonstrated that $FePO_4$ catalyst gradually dissolves in the hot solution (temperature >170 °C) and acts as a homogeneous catalyst. When reaction is over, it can be precipitated as a solid, which is very conducive to the catalyst recovery and circulation. The catalyst still showed good catalytic effect after

5 cycles. The results also showed that $FePO_4$ contained both Brønsted acid and Lewis acid sites with better stability and catalytic performance, so it has good commercial application prospect. Kim et al. (2016) developed the low acid hydrothermal (LAH) fractionation for the effective recovery of hemicellulosic sugar (mainly xylose) from Miscanthus sacchariflorus Goedae-Uksae 1 (M. GU-1). In the first step, the xylose yield was maximized at 75% when the M. GU-1 was fractionated at 180 °C and 0.3 wt% of sulfuric acid for 10 min. In the second step, the furfural yield was achieved at 54% based on the xylan loss in hydrolysate at 180 °C for 30 min.

Sulfuric acid is the traditional catalyst during furfural production. To further improve its efficiency, some process conditions were adjusted. Mazar et al. (2017) investigated the production of furfural from hardwood (aspen and maple chips) pre-hydrolysates used a Parr reactor. The authors found that the adding time of sulfuric acid influenced the furfural yield. Sulfuric acid added when the desired temperature was achieved improved the furfural yield (76%) compared to its addition at the beginning of the reaction (65%). It was also found that recovering furfural by vapor phase as soon as it was formed improved the furfural yield (65%) compared to the case where furfural remained in the reaction medium (54%). Liu et al. (2018) used the vapor-releasing reactor system to separate the furfural from the reaction media, and the maximum furfural yield of 73% was achieved at 200 °C from hydrolysate of hardwood chips. Therefore, the process conditions are important and should be considered in the industrial furfural production processes.

## 13.5 The Formation Mechanism of Furfural

The basic route of preparing furfural from lignocellulosic biomass by hydrolysis method is shown in Fig. 13.5. There are three basic processes: dissolution of hemicellulose from biomass, hydrolysis of hemicellulose to xylose, and dehydration of xylose to furfural. Hemicellulose can be hydrolyzed into pentose in the presence of acid and water, and then xylose is further isomerized and dehydrated to furfural. Furfural continues hydration or resinification due to its unstable properties, it also reacts with xylose and intermediates to form insoluble humins, especially when the reaction conditions are severe (Dussan et al. 2013).

### 13.5.1 Hydrolysis Mechanism of Hemicellulose

Hemicellulose is easier to hydrolyze than cellulose and lignin, so lignocellulose is generally hydrolyzed by dilute acid to dissolve hemicellulose from the cell wall of lignocellulosic biomass. With the participation of dilute acid, the hydrate hydrogen ion ($H_3O^+$) formed by the combination of $H_2O$ and $H^+$ dissociated in water, which can make the oxygen atoms of glycoside bond of hemicellulose be protonated rapidly to form conjugated acid, resulting in the breaking of glycosidic bonds to form carbocations, which then react with $H_2O$ to form monosaccharides (Mamman

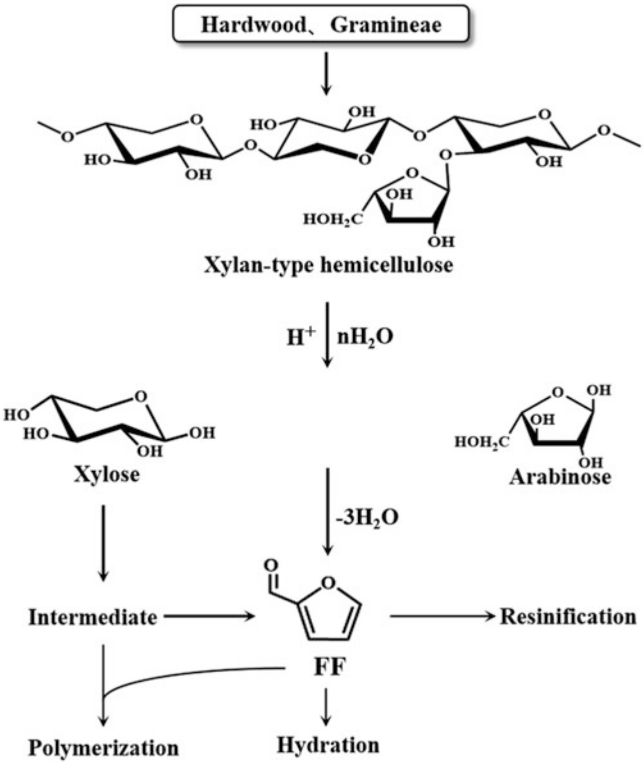


**Fig. 13.5** Main reactions and side reactions in furfural production

et al. 2008; Mäki-Arvela et al. 2011). Hemicellulose is thus hydrolyzed by dilute acid and separated from biomass. The xylan chain is first decomposed into xylo-oligosaccharides and then into xylose monomers, the reaction condition needed is mild and the reaction rate is fast.

The hydrolysis mechanism of hemicellulose to pentose can be summarized as follows (Kapu and Trajano 2014): (1) glycosidic oxygen or ring oxygen is protonated under the action of H$^+$ to form positive oxygen; (2) the glycosidic bond or sugar ring break, forming hydroxyl at one end and carbocation at the other; (3) carbocation reacts with water to form hydronium ion, which then changes to hydroxyl and releases hydrogen ions to continue attacking the remaining glycosidic oxygen or ring oxygen until hemicellulose is completely hydrolyzed into monosaccharides, as shown in Fig. 13.6.

### 13.5.2 Dehydration Mechanism of Xylose to Furfural

The monomeric sugar units of pentosan in lignocellulosic biomass are mainly xylose, and a certain amount of arabinose. The ratio of xylose to arabinose is 10/1

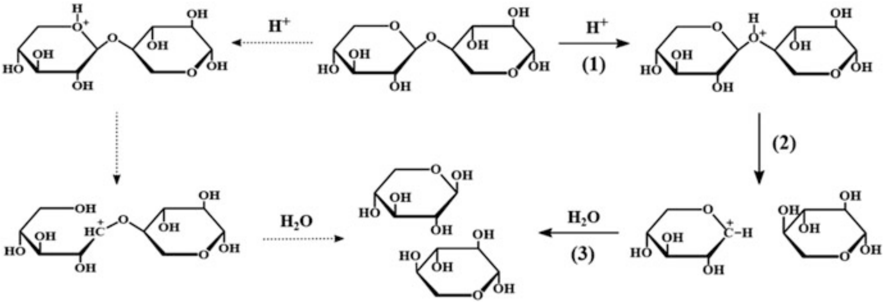


**Fig. 13.6** Proposed hydrolysis mechanism of hemicellulose (pentosan) (Kapu and Trajano 2014). The dominant pathway is shown with solid lines

in rice straw, 52/3.2 in reed, and 10/1 to 20/1 in corn stalk (Yang 2001). The formation mechanism of furfural from arabinose is similar to that of xylose, but the reaction rate is much slower than xylose. Therefore, the formation mechanism of furfural from pentose is usually studied with xylose as reactant.

Furfural is obtained from xylose by isomerization and removal of three molecules of water in acidic condition. The formation for furfural from xylose can be start from the protonation at O-pyranose, C1-OH or C2-OH. Different protonation positions lead to different degradation mechanisms of xylose, resulting in the aldehyde group carbon of furfural derived from C1 or C5 of xylose (Ahmad et al. 1995; Rasmussen et al. 2014). The furfural formation from xylose is complex and may not occur according to one mechanism only. Both the acyclic mechanisms (ring opening of xylose) and cyclic mechanisms have been suggested for the degradation of xylose to furfural.

#### 13.5.2.1 Cyclic Mechanism for Furfural Formation from Xylose

The cyclic dehydration mechanism was first proposed by Antal et al. in 1991. In this pathway, the aldehyde carbon of furfural comes from the C1 of xyose (Antal et al. 1991; Nimlos et al. 2006). The main ideas are as follows: under acidic conditions, xylopyranose directly removes a molecule of water to form a 2,5-anhydride intermediate; the intermediate continues to remove two molecules of water and finally completes the conversion of xylose to furfural. The formation of 2,5-anhydride intermediate from xylose is a crucial step in the formation of furfural. Two reaction paths have been proposed: (1) the combination of hydrogen protons with the oxygen in the C1-OH of xylose; (2) the combination of hydrogen protons with the oxygen in the C2-OH of xylose. The specific conversion process from xylose to furfural is shown in Fig. 13.7.

Protonation of C1-OH. The specific process of the first reaction pathway is that $H^+$ attacks hydroxyl oxygen at C1 position, and then form a carbocation by elimination of the Cl hydroxyl group; the positive charge of C1 site is transferred to the oxygen atom of xylose ring to form oxygen positive ion; subsequently, the C5-O5 bond is broken by the substitution of O2 at C5, and an intermediate structure

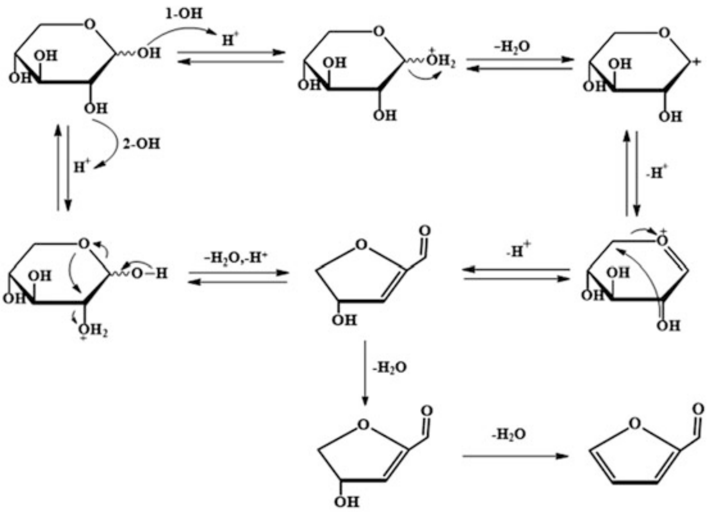


**Fig. 13.7** Cyclic mechanism of furfural formation from xylose by C1-OH and C2-OH protonation (Antal et al. 1991; Rasmussen et al. 2014)

containing furan ring and aldehyde group is formed; finally, the intermediate is dehydrated to form furfural.

Protonation of C2-OH. The specific process of the second reaction route is that $H^+$ first combines with the hydroxyl oxygen at C2 position, and then form a carbocation by elimination of the C2 hydroxyl group; the nucleophilic substitution reaction of O5 containing lone pair electrons at C2 position occurs; at the same time, the O5-C1 bond is broken to form an intermediate containing furan ring and aldehyde group; the intermediate is dehydrated to form furfural. The mechanism of C2-OH protonation is more suitable to explain the formation of furfural in mild hot acidic solution.

### 13.5.2.2 Acyclic Mechanism for Furfural Formation from Xylose

#### 13.5.2.2.1 Protonation of Ring Oxygen (O5)

The mechanism of ring opening dehydration was first proposed by Feather and Harris (1973). It is considered that the ring xylose and the chain xylose are in equilibrium in the reaction process. Xylose is first converted into a chain intermediate by ring opening step, which is then dehydrated and cyclized to form furfural. Some researchers suggested that xylose could open the ring by protonation of the ring oxygen, the specific steps are shown in Fig. 13.8. $H^+$ attacks the ring oxygen of xylose, resulting in ring opening and the formation of 1,2-enol intermediate by enolization. Then enol intermediate are formed through the step-by-step dehydration reaction, and finally dehydrated to furfural (Feather et al. 1972; Ahmad et al. 1995; Rasmussen et al. 2014). In this pathway, the aldehyde carbon of furfural comes from C1 of xylose. Since then, some studies have also suggested that xylose can be directly dehydrated to form 2,3-unsaturated aldehyde via β-elimination, without

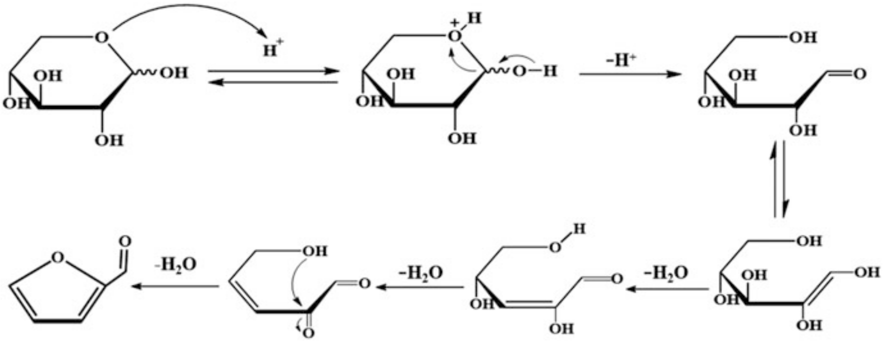


**Fig. 13.8** Acyclic mechanism of furfural formation from xylose by O5 protonation (Feather and Harris 1973; Ahmad et al. 1995; Rasmussen et al. 2014)

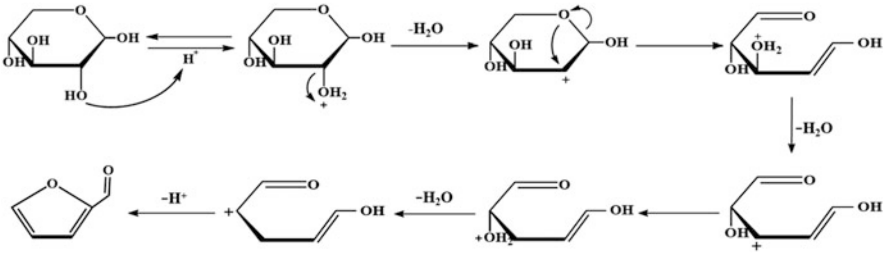


**Fig. 13.9** Acyclic mechanism of furfural formation from xylose by C2-OH protonation

enolization and then further dehydrated to form furfural (Hurd and Isenhour 1932; Danon et al. 2013).

#### 13.5.2.2.2 Protonation of C2-OH

Another accepted path of xylose ring opening dehydration is shown in Fig. 13.9 (Li 2009). Under acidic conditions, $H^+$ first combines with hydroxyl group on C2 and form a carbocation by elimination of the C2 hydroxyl group; then the ring opening reaction of the carbocation occurs to form an aldehyde group and an enolic structure, and furfural is finally formed after dehydration. In this pathway, the aldehyde carbon of furfural comes from C5 of xylose.

The protonation sites and subsequent degradation products were determined by ab initio molecular dynamic simulations in the gas phase and aqueous phase, respectively (Qian et al. 2005a, b; Nimlos et al. 2006; Rasmussen et al. 2014; Antonini et al. 2018). Qian et al. found that in the gas phase, only the protonation at C2-OH led to the formation of furfural, and the protonation at C3-OH led to the fragmentation of xylose (formic acid might be the degradation product). Protonated xyloses at C1-OH and C4-OH are stable (Qian et al. 2005b). In the aqueous phase, the conclusions were similar with that in the gas phase. Qian et al. also suggested that the protonation of hydroxyl groups on the sugar rings was the rate-limiting step for sugar degradation in dilute acid environment (Qian et al. 2005a). Antonini et al. proposed the different reaction mechanism through ab initio molecular dynamic simulations that the formation of furfural from xylose could be started by the protonation at C1-OH in the gas phase (Antonini et al. 2018). Therefore, the theoretical simulation calculation of the formation mechanism of furfural still needs to be supplemented.

#### 13.5.2.3 Mechanism of Furfural Formation from Xylose Catalyzed by Brønsted Acid and Lewis Acid

Xylose has different reaction pathways under the catalysis of Brønsted acid or Lewis acid, as shown in Fig. 13.10. Strong Brønsted acids such as HCl and $H_2SO_4$ are often used as catalysts in industry, and the degradation of xylose follows the direct $H^+$ protonation mechanism (Yang et al. 2012a). In addition, metal chloride and other Lewis acids are often added as catalysts. Differ from Brønsted acid, metal ions with Lewis acidity can coordinate with ring oxygen of xylose to promote ring opening and isomerization of xylose to xylulose (ketose-aldose isomerization process). For example, researchers took $CrCl_3$ as an example to explore the mechanism of furfural formation from xylose catalyzed by $CrCl_3$. With the attack of $Cr^{3+}$ to ring oxygen, xylose is isomerized to xylulose through enolization or 1,2-hydrogen transfer, and then converted into an intermediate with carbonyl carbocation, which is easy to undergo deprotonation to form enol intermediate, and finally lose two molecules of water to form furfural (Binder et al. 2010a). For xylose isomerization, some researchers proposed that xylose could generate enol intermediates through enolization reaction under weak acidic condition, and then be isomerized to xylulose; but under strong acidic conditions, xylulose is directly formed by intramolecular hydrogen transfer (Danon et al. 2013) (Fig. 13.11).

Some researchers have also studied the catalytic reaction of xylose with different Lewis acid (Sn-beta zeolite) and Brønsted acids (HCl and Amberlyst-15) (Choudhary et al. 2012). The results showed that, in addition to the isomerization of xylose to xylulose, the epimerization of xylose to lyxose also happened in the furfural production process under the catalysis of Lewis acid.

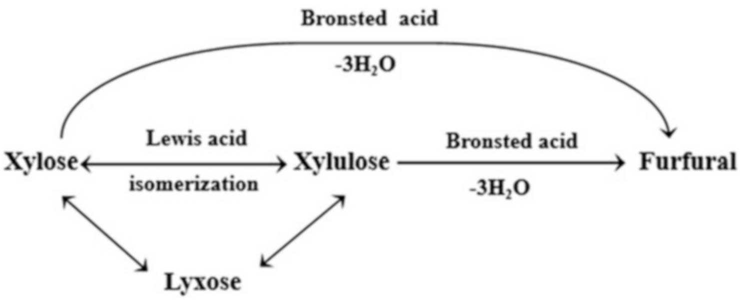


**Fig. 13.10** Effect of Brønsted acid and Lewis acid on reaction pathway

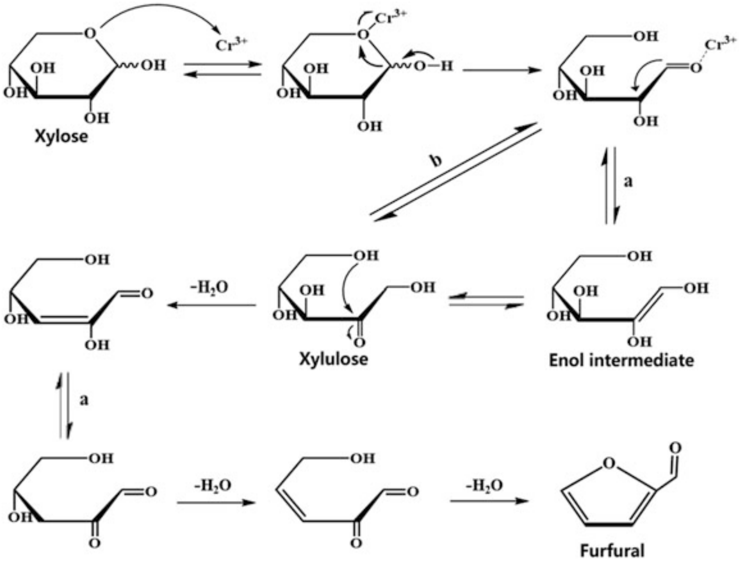


**Fig. 13.11** Mechanism of furfural formation from xylose catalyzed by Lewis acid $CrCl_3$ (**a**) enolization; (**b**) 1,2-hydrogen transfer (Binder et al. 2010a; Danon et al. 2013)

## 13.6 Synthesis of 5-Hydroxymethylfurfural (5-HMF) from Hemicellulose

### 13.6.1 Properties of 5-HMF

5-Hydroxymethylfurfural (5-hydroxymethyl-2-furfural, 5-HMF) is dark yellow needle-like crystal, powder or liquid. It is easily soluble in water, methanol, ethanol, acetone, ether, benzene, etc., while slightly soluble in tetrachloride, insoluble in petroleum ether. 5-HMF has strong hygroscopicity and easy to react with strong oxidant, strong alkali, and strong reducing agent, so it needs to be sealed at low temperature away from light. The physical properties of 5-HMF are shown in Table 13.10.

5-HMF contains a furan ring and the functional groups of hydroxymethyl and aldehyde, making the chemical properties of 5-HMF very active. Many high value-added derivatives can be synthesized from 5-HMF by a series of reactions such as oxidation, dehydrogenation, hydrogenation, halogenation, esterification, and hydrolysis (Kong et al. 2018; Xiao et al. 2018). As shown in Fig. 13.12, 5-HMF can be ring-opened and hydrogenated to obtain 1,6-hexanediol (HDO), which is an important raw material for the synthesis of caprolactone and caprolactam; the C=O bond and C-O bond of 5-HMF can be hydrogenated to obtain 2,5-dimethylfuran (DMF) with similar gasoline characteristics, and 2,5-dimethyltetrahydrofuran (DHMF) can be obtained by further hydrogenation; 5-ethoxymethylfurfural (EMF) can be

**Table 13.10** Physical properties of 5-HMF

| Basic properties | 5-HMF |
|---|---|
| Molecular formula | $C_6H_6O_3$ |
| Molecular weight | 126.116 |
| Melting point (°C) | 28–34 |
| Boiling point (°C) | 114–116 |
| Density (g/mL) | 1.234 (25 °C) |
| Refractive index | 1.562 (20 °C) |
| UV absorption wavelength (nm) | 284 |

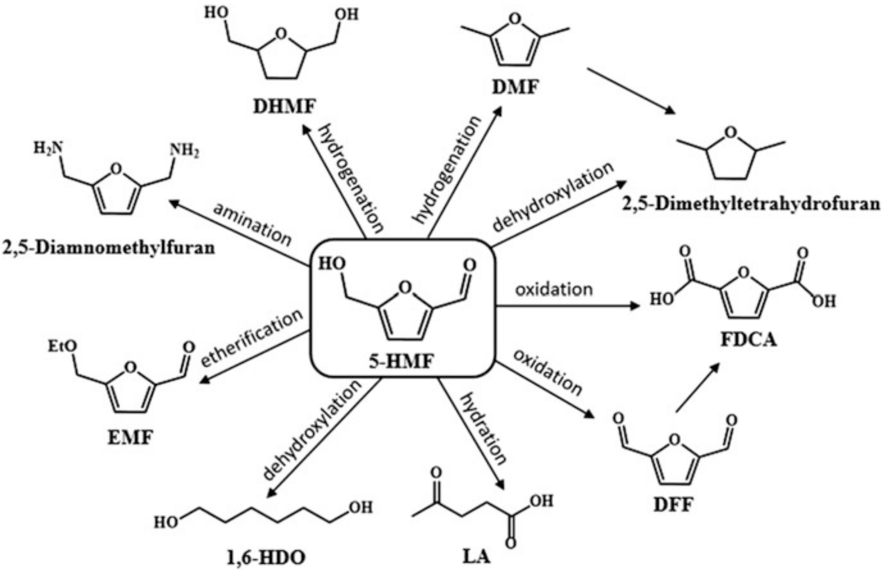


**Fig. 13.12** 5-HMF and its derivatives

obtained by etherification from 5-HMF; 2,5-furanedioic acid (FDCA) and 2,5-diformylfuran (DFF) can be obtained by oxidation; 2,5-diamnomethylfuran can also be prepared by amination reaction. As an important biomass-based platform compound, 5-HMF can be used as an intermediate in many reactions to prepare a variety of polymer materials, high value-added chemicals, biofuels, and additives, etc., and has been widely used in fields of chemical, energy, material, and medicine (Wang et al. 2008; Van Putten et al. 2013b).

## 13.6.2 Production of 5-HMF from Hemicellulose Derived Sugars

Sugar compounds are the main source for the preparation of 5-HMF, which can be divided into monosaccharides, oligosaccharides, and polysaccharides. Among them, fructose and glucose as representative monosaccharides are the most widely studied;

cellulose, starch, and chitosan are the common polysaccharides to prepare 5-HMF (Wang 2018; Li et al. 2020). In addition, hexose in hemicellulose can also be used to prepare 5-HMF, such as mannose, galactose, and glucose. Hexose is abundant in coniferous wood, among which the monosaccharide of hemicellulose is mainly mannose. For example, mannose accounts for about 10% of dry weight in pine, and the ratio of galactose, glucose, and mannose is 0.1–1:1:3 (Wei et al. 2011). Glucose, mannose, and galactose, have very similar molecular structures; mannose and galactose are C-2 and C-4 epimers of glucose, respectively (Yang 2001; He 2019). There are mature technology and equipment for the preparation of 5-HMF from glucose (the upstream raw material is mainly cellulose), but there are few reports from mannose and galactose. Therefore, the progress of preparing 5-HMF with mannose from hemicellulose as raw material is mainly introduced, which will be beneficial to the better utilization of hemicellulose. The preparation process is similar to that of glucose, which is influenced by catalyst type, solvent system (monophasic system and biphasic system), and process strengthening method (microwave heating and supercritical heating).

Seri et al. studied the formation of 5-HMF from glucose, fructose, mannose, and galactose using lanthanide chloride as catalyst in water, respectively, and it was found that the yield of 5-HMF from fructose was significantly higher than that of glucose, mannose and galactose. Therefore, it was concluded that ketose could gain a higher 5-HMF yield than that of aldose (Seri and Sakaki 1996, 2002; Seri et al. 2001). Glucose, mannose, and galactose are aldohexoses, which might be isomerized to hexulose (such as fructose) and then converted to 5-HMF (Bhanja et al. 2017). The isomerization process is the most critical step, which needs the presence of Lewis acid or Lewis base. Some researchers have found that mannose is mainly isomerized to fructose, which can be converted into 5-HMF efficiently, while galactose tends to isomerize to tagatose, which is the C-4 epimer of fructose (Fig. 13.13) (De et al. 2012; Van Putten et al. 2013a). However, the dehydration activity of tagatose to produce 5-HMF is weaker than that of fructose, leading to the lower yield of 5-HMF from galactose than mannose.

De et al. (2012) designed porous solid catalyst $TiO_2$-H ($TiO_2$ prepared by hydrothermal method) containing strong Lewis acidic sites for the production of

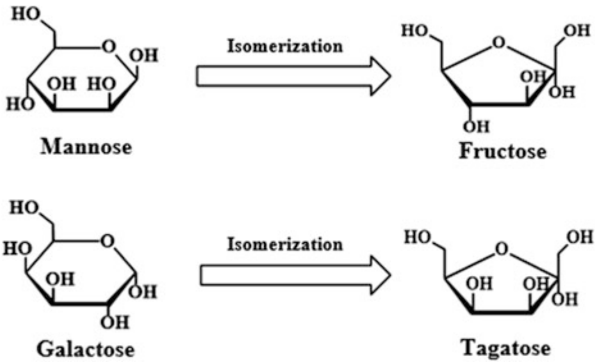


**Fig. 13.13** Isomerization of mannose and galactose

5-HMF from mannose, lactose, and galactose. Dehydration reaction of 25 mg mannose with 10 mg $TiO_2$-H catalyst produced 44% HMF under microwave irradiation for 5 min in DMA–LiCl medium at 140 °C. At the same conditions, the 5-HMF yields from lactose and galactose were 35% and 27%, respectively, which indirectly indicated that mannose was easier to form 5-HMF than lactose and galactose. When the homogeneous catalyst $CrCl_2$ is used in the DMA-LiCl system, 54% 5-HMF could be obtained from mannose at 100 °C for 2 h (Binder et al. 2010b). Replacing the additive of LiCl to LiBr under the same conditions, the yield of HMF increased to 69%. When the DMA-LiCl system is changed to ionic liquid [EMIM]Cl, the yield of HMF is 68% from mannose at 100 °C for 2 h (Binder et al. 2010b). The results proved the synergistic effect of the solvent system and catalyst.

Organic solvents, such as DMSO, GVL, and DMA, do not contain $H^+$, which can reduce the degradation of HMF, thus increase the yield of HMF. Bhanja et al. (2017) prepared a bifunctional solid catalyst MPBOS with molecular sieve SBA-15 as a carrier to catalyze mannose in DMSO at 135 °C for 20 min, and the HMF yield reached 61%. The combination of two kinds of catalysts is also an effective method for preparing 5-HMF. Wrigstedt et al. (2016) used Amberlyst-38 and $CrCl_3 \cdot 6H_2O$ as catalysts, potassium bromide (KBr)-GVL as solvent system, yielding 69% 5-HMF at 160 °C for 3 min with the assist of microwave. Therefore, choosing an appropriate catalyst or solvent system is a more effective way to convert mannose into 5-HMF. At present, there is still a lack of a relatively low-cost 5-HMF preparation method, which limits its industrial production and application.

Some researchers conducted reaction kinetics studies on glucose, mannose, and galactose (Chen et al. 2016). They found that higher reaction temperature promoted the degradation of hexose and the generation of 5-HMF. At the temperature of 200 °C, the conversion rate of hexose can be more than 90%; while galactose is easily isomerized to produce tagatose instead of fructose, resulting in the highest HMF yield of 23%, which is lower than that of mannose (27%). The authors established a two-step parallel reaction kinetic model, in which 5-HMF and humins were generated in parallel from hexose, while levulinic acid (LA) and humins were generated in parallel from 5-HMF. The model was used to predict the degradation process of hexose (Fig. 13.14) by analyzing the kinetic parameter ($k$) of mannose and galactose at different reaction temperature (T) (Fig. 13.15). As the T increased, the $k_1$ and $k_2$ values of hexoses showed a gradual increment, indicating that the increase of T promoted the reaction of hexoses, and the production of humins increased correspondingly when HMF increased. Additionally, $k_1/k_2$ values gradually increased with the increase of T, but less than 1, indicating that the influence of T on the generation of 5-HMF become increasingly significant than that of humins. In contrast, the value of $k_1/k_2>1$ for glucose at 200 °C, demonstrating that glucose tended to produce 5-HMF rather than humins at high temperature, while mannose and galactose tend to aggregate to form humins. It is also found that the value of $k_3/k_4$ was always less than 1, indicating that 5-HMF was more likely to form humins by polymerization at high temperature. $k_2$ and $k_4$ represented the formation rate of humins from hexoses and 5-HMF, respectively. It could be found that $k_2$ and $k_4$ of mannose were relatively close, indicating that the humins are generated through

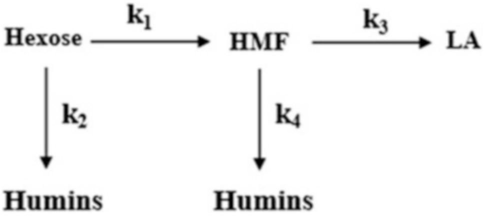


**Fig. 13.14** Hexose degradation model (Chen et al. 2016)

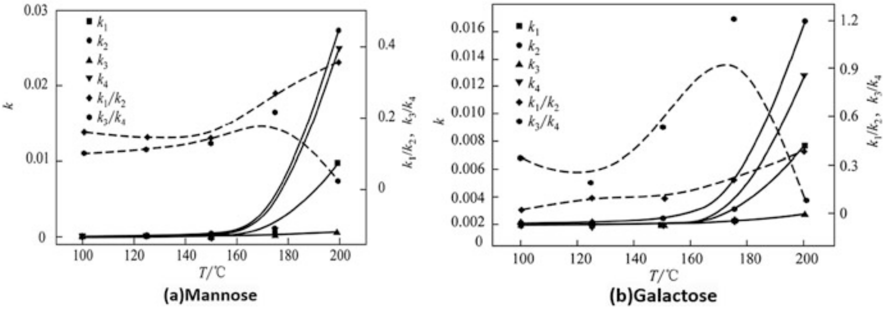


**Fig. 13.15** (**a**, **b**) Kinetic constants of reaction of mannose and galactose at different temperature (Chen et al. 2016)

mannose polymerization and HMF polymerization; while the $k_2$ of galactose is greater than $k_4$, which indicatedthe formation of humins is mainly through the polymerization of galactose.

Monosaccharides do not naturally exist, but are stored in lignocellulosic biomass in the form of sugar units. Hydrolysate of lignocellulosic biomass contains a variety of monosaccharides, including hexose. Due to the complexity of lignocellulosic biomass composition, the co-degradation of cellulose, hemicellulose, and other monosaccharide components should be considered in the preparation of 5-HMF. The existing researches on the conversion of hexose to 5-HMF is not enough to study the hemicellulose in lignocellulosic biomass. When lignocellulosic biomass was used as raw material, cellulose was preferentially degraded to 5-HMF than hemicellulose. The existing researches on improving the yield of 5-HMF was always aimed at improving the conversion of cellulose to 5-HMF, while the conversion of hemicellulose to 5-HMF was relatively low (van Putten et al. 2013a; Wang et al. 2014a; Menegazzo et al. 2018).

### 13.6.3 Formation Mechanism of 5-HMF from Hexose

5-HMF is formed by dehydration of hexose with the presence of acid catalyst. There are four reactions in the conversion of hexose to 5-HMF, including isomerization, dehydration, fragmentation, and condensation (Dussan et al. 2013; Liu et al. 2020).

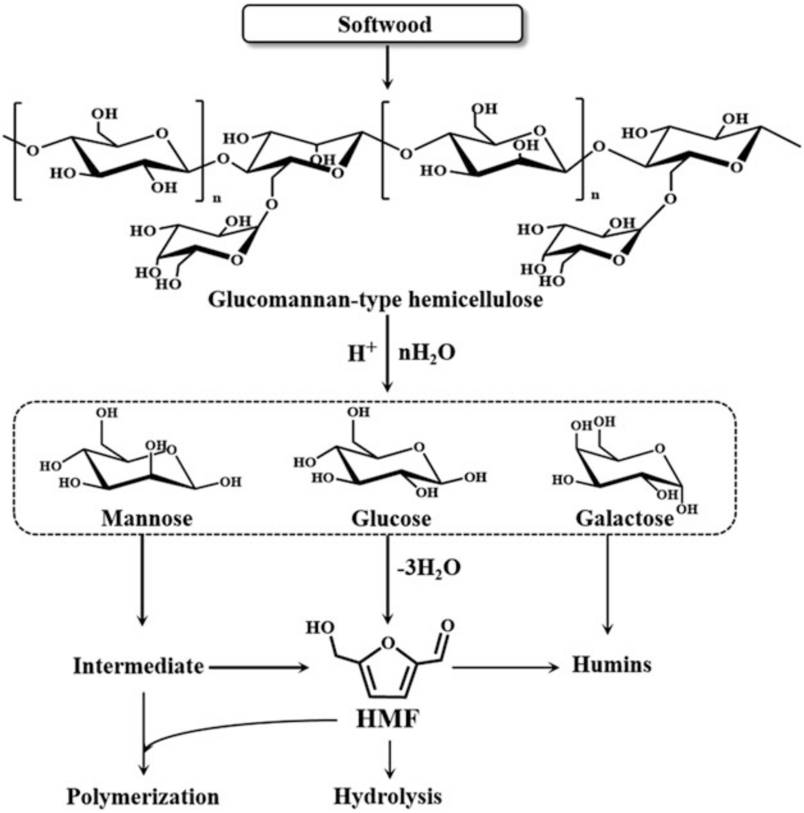


**Fig. 13.16** Main reactions and side reactions of 5-HMF formation

Hexose in hemicellulose mainly includes mannose, glucose, and galactose. The pathway of these hexoses to form 5-HMF can be roughly divided into two steps: Hexoses are firstly isomerized to fructose; then fructose is dehydrated to form 5-HMF. In the process of 5-HMF formation, many side reactions occur in acidic solution due to the active functional groups of hexose, such as aldol condensation, molecular isomerization, pyrolysis, hydration, cross polymerization, resulting in the formation of many by-products. For example, some soluble polymers and insoluble humins will be generated during the dehydration of reaction intermediates; meanwhile, 5-HMF will be further hydrolyzed to produce levulinic acid and formic acid in acidic water environment (Fig. 13.16). These by-products greatly affect the yield of 5-HMF.

#### 13.6.3.1 Formation Mechanism of 5-HMF from Fructose

In the middle of the twentieth century, Haworth first proposed a catalytic reaction mechanism for the 5-HMF formation from fructose (Haworth and Jones 1944; Liu 2015), but until now, there is still no authoritative conclusion on the dehydration

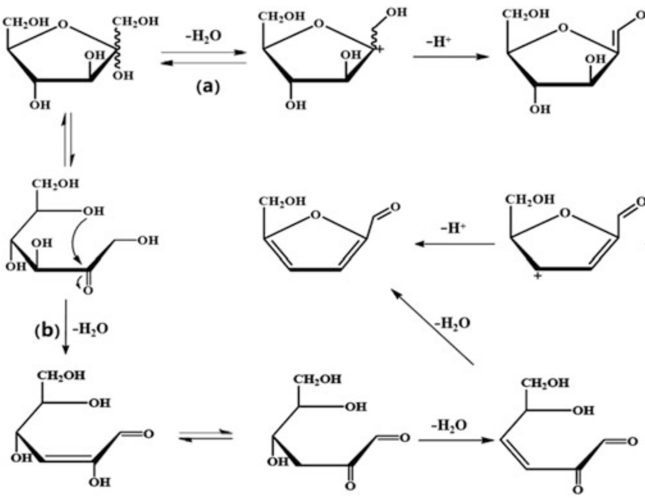


**Fig. 13.17** Formation mechanism for 5-HMF from fructose

conversion mechanism of fructose in the world. Under acidic conditions, hexose molecules can form 5-HMF by the elimination of three molecules of water. There are two main accepted mechanisms, cyclic dehydration mechanism and acyclic dehydration mechanism, as shown in Fig. 13.17 (Dam et al. 1986; Antal Jr et al. 1990): (a) Fructose first remove one molecule water to form enol intermediate (cyclopentanone furanose), and then remove two molecules of water to form 5-HMF; (b) Fructose is isomerized to 1,2-enediol, and one molecule water is removed to form 3-deoxyglucosone, then 5-HMF is obtained by further removing two molecules of water. Moreau, feather, and Harris agreed that the key step in the formation of 5-HMF was the dehydration of hexose to 3-deoxyglucosone (Moreau et al. 1996).

#### 13.6.3.2 Formation Mechanism of 5-HMF from Aldose

Mannose is the C-2 isomer of glucose, the mechanism of mannose to 5-HMF is similar to that of glucose to 5-HMF (Binder et al. 2010b). Both of them are isomerized to ketose (fructose), and fructose is further dehydrated to 5-HMF. The mechanism of glucose dehydration to HMF is the most studied. Glucose has a stable pyran ring structure, which makes the conversion process of glucose into HMF more difficult than that of fructose, and the mechanism is also more complex. According to C2-OH or O5 protonation, cyclic dehydration mechanism and acyclic dehydration mechanism were proposed, respectively (Rasmussen et al. 2014). Each of mechanisms can further occur either through isomerization to produce fructose or by not producing fructose.

The cyclic dehydration mechanism is initiated by C2-OH protonation. In the presence of strong Brønsted acid, glucose directly removes the three molecules of water to form 5-HMF via a furanose secondary carbocation with no isomerization to

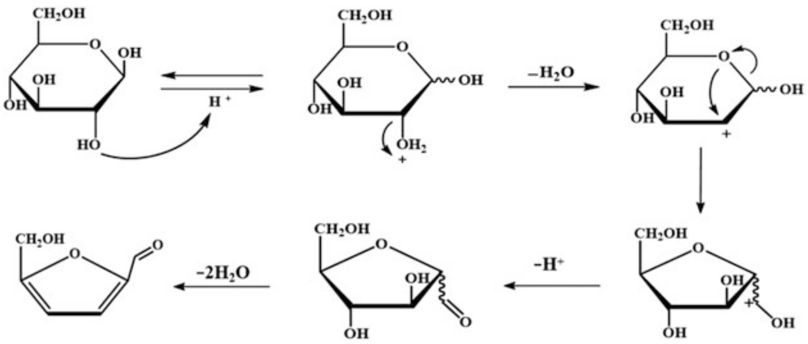


**Fig. 13.18** Cyclic mechanism of 5-HMF formation from glucose without isomerization

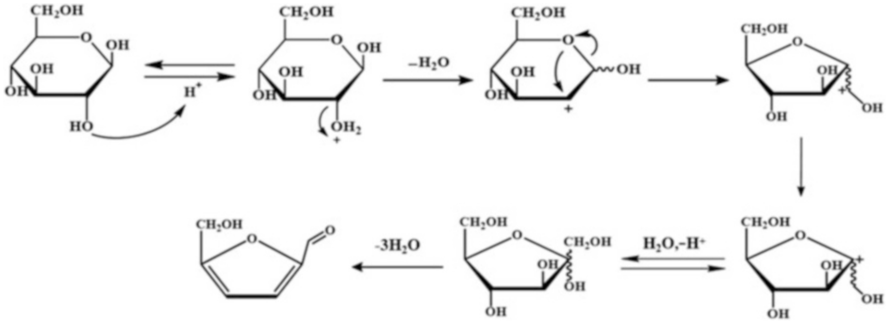


**Fig. 13.19** Cyclic mechanism of 5-HMF formation from glucose with isomerization

fructose (Fig. 13.18) (Qian 2012). Conversely, in the presence of appropriate Lewis acid or isomerase or base, glucose will be first enolized and isomerized into fructose, then removed one molecule of water to form a ring structure, and 5-HMF will be generated by dehydration cyclization, as shown in Fig. 13.19 (Akien et al. 2012).

The acyclic dehydration mechanism is initiated by ring oxygen (O5) protonation which leads to ring opening. Some studies have shown that the preparation of 5-HMF from hexose is more suitable to be explained by ring opening mechanism. Ring opening is followed by either the isomerization to fructose or aldose conversion process, in which case the compounds are dehydrated further through a series of steps to produce 5-HMF (Binder and Raines 2009; Chen and Lin 2010; Ren et al. 2013). There are two isomerization mechanisms of glucose to fructose (Fig. 13.20): (a) ring-opened glucose first forms the 1,2-enediol through enolization, then isomerized to fructose; (b) the proton transfer between C1 and C2 of glucose results in the exchange of aldehyde group and hydroxyl group, resulting in fructose formation, which can be named as 1,2-hydrogen transfer (Paine et al. 2008; Yang et al. 2012c).

Glucose additionally follows an acyclic mechanism with no fructose intermediate and directly to 5-HMF (Antal et al. 1991). In the presence of acid catalyst, the enol

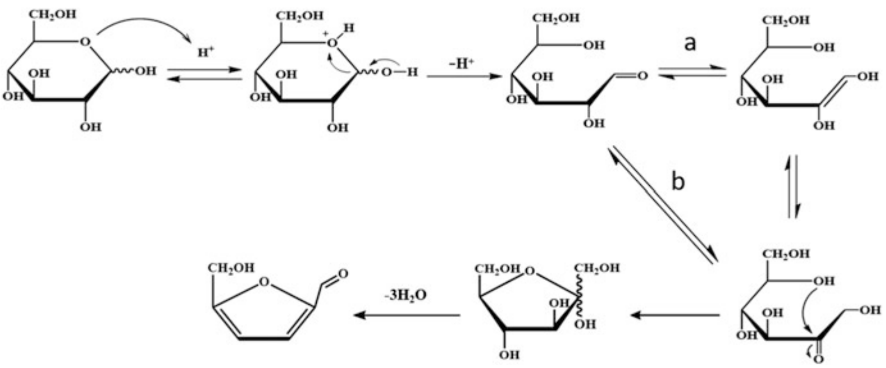


**Fig. 13.20** Acyclic mechanism of 5-HMF formation from glucose through fructose with isomerization: (**a**) enolization; (**b**) 1,2-hydrogen transfer

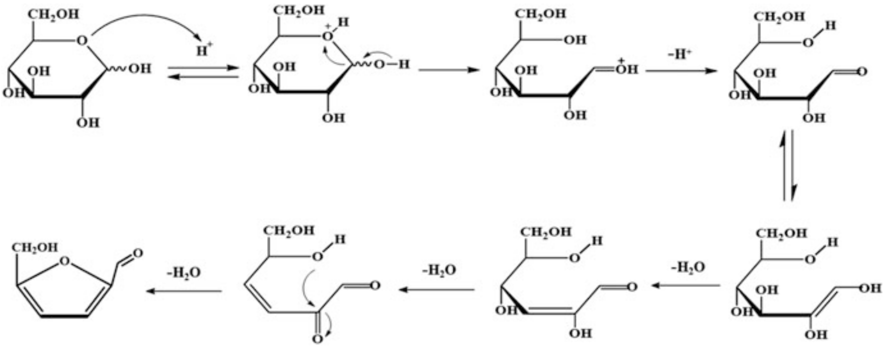


**Fig. 13.21** Acyclic mechanism of 5-HMF formation from glucose with no fructose intermediate

isomerization of glucose occurs first, and then the hydroxyl groups at C3 and C4 are gradually removed to form deoxyglucosone products. 5-HMF is formed after dehydration and ring reclosure (Fig. 13.21).

In general, the reaction mechanism of hexose to 5-HMF is complex, which is related to the reaction system, and there are different opinions about the mechanism at present. With the continuous development of detection methods, it is believed that the mechanism of hexose to 5-HMF will be finally concluded, which requires the mutual efforts of many researchers.

**Acknowledgements** This work was supported by the grants from National Natural Science Foundation of China (No. 21978104), Guangdong Basic and Applied Basic Research Foundation (No. 2019A1515011654), and State Key Laboratory of Pulp and Paper Engineering (2020ZR04 and 202106).

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# Biomedical and Pharmaceutical Applications of Xylan and Its Derivatives

# 14

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## Abstract

Hemicelluloses are non-soluble plant cell wall polysaccharides that can be separated by alkali or hydrolyzed by dilute acids. Major hemicelluloses are xylan, glucuronoxylan, arabinoxylan, mannan, glucomannan, and galactoglucomannan. The non-toxicity, abundance, and biodegradability of hemicelluloses make it a prospective substrate for the production of oligosaccharides and other value-added products that are used in biomedical and pharmaceutical fields. Xylooligosaccharides can be produced by enzymatic hydrolysis of xylan extracted from agro-waste and have applications in blood sugar level control, boosting immunity, improving intestinal function, and reducing fatigue. Other derivatives like xylan esters and xylan ethers function as anticoagulants and inhibit the growth of harmful bacteria. Xylan-based materials like hydrogels and biofilms are effective in cell immobilization, wound dressing, cancer therapy, drug delivery, prevention of neurodegenerative, cardiovascular disease and treatment of various chronic diseases.

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M. Brienzo (ed.), *Hemicellulose Biorefinery: A Sustainable Solution for Value Addition to Bio-Based Products and Bioenergy*, Clean Energy Production Technologies, https://doi.org/10.1007/978-981-16-3682-0_14

**Keywords**

Xylooligosaccharide · Hemicellulose · Hydrogels · Cell immobilization · Cancer therapy

## 14.1 Introduction

Lignocellulosic waste from agriculture and forest residues comprises mainly cellulose, hemicellulose, and lignin (Machado et al. 2016). Hemicellulose is the second most abundant polymer and is the structural component of the plant cell wall (Eriksson 1990). It constitutes around 15–35% of lignocellulosic biomass (Limayem and Ricke 2012). Hemicellulose comprises a highly branched polymer of C5 sugars (glucuronoxylan and arabinoxylan) and C6 sugars (xyloglucan and mannan) (Negahdar et al. 2016). The highly branched structure and amorphous nature of hemicellulose enables its easy conversion into value-added compounds like xylitol, xylooligosaccharides (XOS), etc. (Sharma et al. 2020a). The monosaccharides from hemicellulose have different applications in the production of alcohol, biofuels, antibiotics, and therapeutic products (Banerjee et al. 2018a, b). The agriculture and industrial waste containing hemicellulose serve as renewable and sustainable renewable resources to fulfill human demands (Anwar et al. 2014). Agriculture crops like sugarcane, rice, wheat bran, maize, sweet potato, corn, and forest residues are some of the examples of potential hemicellulosic sources (Isikgor and Becer 2015). In 1891, Schulze isolated hemicellulose from plant biomass for the first time by using dilute alkali and found that it comprises different monosaccharide moieties (Sharma and Kumar 2013). Hemicelluloses are structural polysaccharides, which are closely associated with cellulose and lignin and play an important role in maintaining rigidity in lignified tissues of plant cell walls (Coomey et al. 2020). Some examples of hemicelluloses are xylan, arabinans, glucuronoxylan, and arabinoglucuronoxylan (da Silva et al. 2012). This chapter is focused on the applications of extracted xylan and its derivatives in biomedical and pharmaceutical fields.

### 14.1.1 Xylan

Xylan is the most abundant hemicellulose polysaccharides found in hardwood and herbaceous biomass consisting of β-D-xylopyranosyl (xylose) residues linked by β-1-4 glycosidic bonds (Machado et al. 2016). Xylans can be further categorized as homo- or heteroxylans based on the presence of the side chain. Heteroxylans are associated with various functional groups, such as 4-*O*-methylglucuronic acid, glucuronic acid, arabinose, galactose, and glucose (Zhou et al. 2017). Heteroxylans are classified as glucuronoxylans, arabinoxylans, arabinoglucuronoxylans, and glucuronoarabinoxylans based on the structure and abundance of the side chains (Van Dyk and Pletschke 2012). The potential sources of xylan are agriculture residue, waste products from hardwood and softwood (Singh et al. 2017). Xylan extracted from corn cob has a promising application in the development of colon-specific drug carriers in the treatment of colon cancer (da Silva et al. 2012).

#### 14.1.1.1 Homoxylan

Homoxylans are a linear chain of xylose units comprising β-1,4-D-xylan, β-1,3-D-xylan, and β-1,3:1,4-D-xylan (Cordeiro et al. 2015). Homoxylans with β-1,3 linkage are found in green algae, whereas homoxylans with mixed β-1,3 linkage and β-1,4 linkage are found in red seaweeds of *Palmariales* and *Nemaliales* (Fu et al. 2019). Homoxylans with β-1,4 linkage are found in higher plants substituted with *O*-acetyl group (Zhou et al. 2017). Homoxylans are extracted from sources such as seaweeds, buriti fruits, and plant seeds (Cordeiro et al. 2015).

#### 14.1.1.2 Arabinoxylan

Arabinoxylans are the major hemicellulose polysaccharides of herbaceous biomass such as wheat grain, rye, corn, barley, and oat (Machado et al. 2016). Arabinoxylan is a major component of dietary fiber in cereals (Fadel et al. 2018). Arabinoxylans contain arabinose as mono-substitution at either O-2 or O-3 or di-substitution at O-2 and O-3 positions of β-1,4-linked D-xylopyranose units in the backbone structure (Kaur et al. 2019). Arabinoxylan is of two types based on its solubility in water as water-extractable and unextractable (Tremmel-Bede et al. 2017). Arabinoxylans are used as a food additive, prebiotic nutrients, antioxidants and as therapeutic agents (Yadav et al. 2017; Chen et al. 2019). Arabinoxylan from psyllium is used in a broad range of pharmacological activities such as anti-tumor, anti-inflammatory, anti-diabetic, hypolipidemic, laxative, anti-obesity, anti-diarrheal, and anti-amoebic activity (Hussain et al. 2016). Ferulated arabinoxylans can form covalent gels through the cross-linking of their ferulic acid and these ferulated arabinoxylan gels represent an excellent alternative as colon-targeted drug delivery system (Banerjee et al. 2018a, b). Arabinoxylan also has various biological properties, like reducing cholesterol level in blood serum, immunity-boosting, anticancer, preventing aging (Fadel et al. 2018), neurodegenerative and cardiovascular diseases (Mendez-Encinas et al. 2018).

#### 14.1.1.3 Glucuronoxylan

Glucuronoxylans have xylose units in the backbone structure with 4-*O*-methylglucuronic acid and/or glucuronic acid groups as primary side chain groups (Vignon and Gey 1998). Acetyl groups are attached to the C2 and/or C3 of xylose residues of the backbone. About 70–80% of the xylose units are acetylated at the C-2 or C-3 positions (Bajpai 2018). Glucuronoxylan is used in designing solvent and ionic stress-sensitive oral tablet formulation as it exhibits a high swelling index with stimuli-responsive swelling or de-swelling properties (Muhammad et al. 2020).

#### 14.1.1.4 Glucuronoarabinoxylan or Arabinoglucuronoxylan

Heteroxylans in which xylose residues contain both 4-*O*-methylglucuronic acid (and/or glucuronic acid) groups and arabinose side chains are termed as glucuronoarabinoxylans or arabinoglucuronoxylans (Talmadge et al. 2014).

Glucuronoarabinoxylan showed gastroprotective effect, by reducing gastric hemorrhagic lesions, when orally administered to rats (Simas-Tosin et al. 2014). The conventional and advanced methods for the extraction of xylan from various agriculture sources have been described in the subsequent sections.

## 14.2 Extraction of Xylan

The plant cell wall contains both water soluble and insoluble hemicellulose polysaccharides. In water soluble hemicelluloses, xylan is the major component and glucan and mannan are the minor components (Mikkonen and Tenkanen 2012). The separation of a specific xylan from various agriculture waste can be improved by milling, sieving and pearling or debranning process (Kim et al. 2020). The recalcitrance of lignocellulosic biomass is one of the major challenges encountered in the xylan extraction process due to the physical and chemical bonding within the cell wall components (cellulose and lignin) (Zoghlami and Paës 2019). In the xylan extraction process, the biomass is heated under alkaline conditions that leads to the separation of hemicellulose and de-acetylation of side chain groups. The covalent and non-covalent bonding of hemicellulose with lignin and hydrogen bonding with cellulose can be broken by various pretreatment processes before the extraction step (Sporck et al. 2017). The biomass structure is altered by the pretreatment process that also helps in the cellulose and hemicellulose hydrolysis. The pretreatment step modifies or partially removes the lignin and increases the porosity and surface area of biomass that leads to the improvement in the hydrolysis process (Juárez et al. 2018). For better extraction of xylan, physical, biological, chemical, and physicochemical pretreatment methods have been used (Kocabaş et al. 2020). The pretreatment also contributes to the extended separation and purification steps for xylan extraction. The chemical pretreatment has some disadvantages such as corrosion of reactor and chances of inhibitory effects in the enzymatic hydrolysis process. To overcome these disadvantages, the combination of mild physicochemical pretreatments can be used (de Oliveira Santos et al. 2018). The extraction of xylan by using different processing methods and biomass sources are listed in Table 14.1.

The pretreatment methods involved in the extraction of xylan from various agriculture wastes include autohydrolysis, alkali, hot water hydrolysis, ultrasonication and alkali treatment combined with chlorite solution or hydrogen peroxide or dimethyl sulfoxide. The extracted xylan shows variation in the structures based on different raw material sources and the extraction method used. The monosaccharides such as arabinose, glucose, galactose, mannose, and xylose are found in the hydrolyzed xylans (Egüés et al. 2013).

**Table 14.1** Xylan extraction from various agriculture wastes

| Raw material | Extraction method | Extraction yield | Reference |
|---|---|---|---|
| Acacia sawdust | 10% NaOH + 1% $H_3BO_4$, 60 °C, 3 h | 23.5% of dry acacia sawdust | Sharma et al. (2020a) |
| Cotton stalks | 24% KOH + 1% $NaHBH_4$ | 20% of total dry cotton stalks | Akpinar et al. (2007) |
| Corn cob | 5% NaOH, 60 °C, ultrasonication, 1 h | 36.1% of original xylan | Hromadkova et al. (1999) |
| Corn cob | Classical extraction, 5% NaOH, 1 h | 31.5% of original xylan | Hromadkova et al. (1999) |
| Corn cob | Ultrasonication, 10 min cycle, 1 h, 25 °C | 52.7% of original xylan | Ebringerova and Hromadkova (2002) |
| Corn cobs | 12% NaOH + Steam | 83% of original xylan | Samanta et al. (2017) |
| Corn stalks | 10% NaOH, 20 °C | 54% of original sugars | Egüés et al. (2012) |
| Green coconut husks | 4% KOH + Steam | 84% of original xylan | Jayapal et al. (2014) |
| Natural grass | 12% NaOH + Steam | 98% of original xylan | Samanta et al. (2012) |
| Neem sawdust | 10% NaOH + 1% $H_3BO_4$, 60 °C, 3 h | 22.5% of total neem sawdust | Sharma et al. (2020b) |
| Pigeon pea stalks | 12% NaOH + Steam | 96% of original xylan | Samanta et al. (2013) |
| Pineapple peel | 10% NaOH, 45 °C, 16 h | 87.6% of total xylan | Banerjee et al. (2019) |
| Poplar wood | 6% NaOH + Sonication | 75.5% of original xylan | Yuan et al. (2010) |
| Sugarcane bagasse | 3% NaOH, 50 °C | 74.9% of original xylan | Peng et al. (2009) |
| Sugarcane bagasse | 12% NaOH + Steam | 85% of original xylan | Jayapal et al. (2013) |
| Sugarcane bagasse | Two-stage extraction with water and 1% NaOH | 49.5% of original xylan | Peng et al. (2010) |
| Sugarcane bagasse | Ultrasonication, 10% (w/v) NaOH, 15 h | 97.3% of total xylan | Ren et al. (2006) |
| Sugarcane bagasse | 40% NaOH, 60 °C, 2 h | 53% of original xylan | Sporck et al. (2017) |
| Sugarcane bagasse | 6% $H_2O_2$, 25 °C 4 h | 80% of original xylan | Alves et al. (2020) |
| Sugarcane tops | 10% NaOH + 1% $H_3BO_4$, 60 °C, 3 h | 25% of raw sugarcane top | Khaire et al. (2021) |
| Sunflower stalks | 24% KOH + 1% $NaHBH_4$ | 18.9% of dried sunflower stalks | Akpinar et al. (2009) |
| Tobacco stalks | 24% KOH + 1% $NaHBH_4$ | 21.8% of dried tobacco stalks | Akpinar et al. (2009) |

(continued)

**Table 14.1** (continued)

| Raw material | Extraction method | Extraction yield | Reference |
|---|---|---|---|
| Wheat straw | 0.5 M NaOH, 55 °C | 49.3% of original xylan | Ruzene et al. (2007) |
| Wheat straw | Ultrasonication, 0.5 M KOH, 30 min | 25.5% of total dried wheat straw | Sun and Tomkinson (2002) |
| Wheat straw | Steam explosion | 80% of total hemicellulose | Hongzhang and Liying (2007) |
| Wheat straw | OrganoSolv | 41% of original xylan | Sun et al. (1998) |
| Wheat straw | 24% KOH + 1% $NaHBH_4$ | 20.6% of dried wheat straw | Akpinar et al. (2009) |

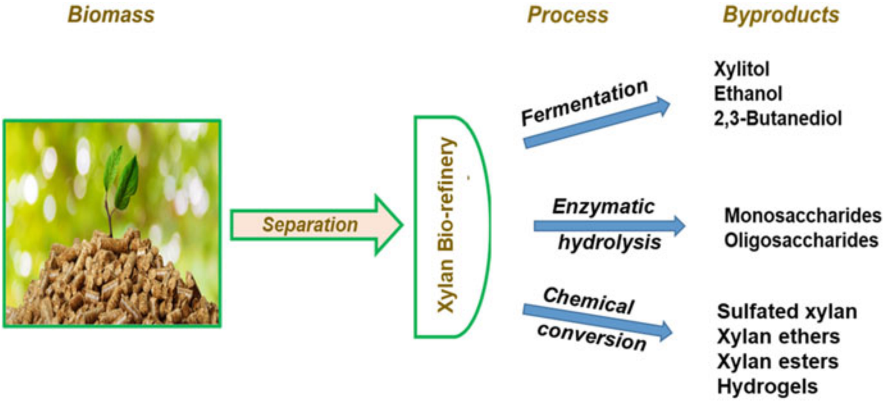

**Fig. 14.1** Xylan biorefinery: process and byproducts

## 14.3 Xylan-Based Biorefineries

The use of lignocellulosic waste has gained interest in recent times from the biorefinery point of view. This is similar to the traditional refinery concept, where several byproducts such as biofuels, chemicals, and other value-added products can be obtained from lignocellulosic biomass (Silva et al. 2020). The xylan biorefinery process and byproducts are shown in Fig. 14.1.

In the xylan biorefinery, the opportunity for profitable implementation is limited due to the high cost requirements in the sequential biomass and product refining process. To overcome this, researchers are exploring to obtain the maximum profit by gaining a higher quantity of product per unit mass of the starting feedstock and this can be possible only if agriculture waste can be used as a feedstock. In the xylan biorefinery concept, high value-added compounds, e.g., oligosaccharides like xylo-, arabinoxylo- and galactoxylo-oligosaccharides and the monosaccharides like xylose and arabinose can be produced by enzymatic hydrolysis of xylan (Otieno and Ahring 2012). The chemicals such as xylitol (Silva et al. 2020), bioethanol (Baêta et al. 2016), and acetic acid (Xavier et al. 2017) can be produced through fermentation of hemicellulosic monosaccharides. The other derivatives such as sulfated xylan, xylan esters, and ethers can be produced through chemical modification of xylan polymers (Petzold-Welcke et al. 2014). Xylan hydrolysis, chemical modification, and fermentation are the three types of methods that can be used to produce abovementioned value-added products from extracted xylan from different biomasses.

### 14.3.1 Hydrolysis of Xylan

The xylan can be hydrolyzed by chemicals or enzymes. The oligosaccharides from xylan can be produced by hydrolyzing the glycosidic bonds in the main chain. This can be achieved by using heat, chemical reagents or enzymes.

#### 14.3.1.1 Xylooligosaccharides Production by Physicochemical Hydrolysis

The production of XOS can be achieved by the hydrolysis of xylan extracted from agriculture waste. Along with the monosaccharides, the byproducts such as furfural can also be obtained from xylan by thermochemical process (Cho et al. 2020). The high concentrations of acid, alkali and hot water hydrolysis pretreatments are not suitable for XOS production rather xylose and furfural are produced as the final products (Cano et al. 2020). Therefore, to avoid the direct hydrolysis of xylan into monosaccharides, the acid concentration should be less than 1% (v/v). The acid concentration higher than 1% releases xylose and other side chain monosaccharides, which can further hydrolyze to give furfural or hydroxy-methyl-furfural (Brienzo et al. 2016; Hilpmann et al. 2016).

#### 14.3.1.2 Xylooligosaccharides Production by Enzymatic Hydrolysis

Xylan from lignocellulosic waste is extracted by a suitable pretreatment method, prior to XOS production by enzymatic hydrolysis. Characteristics of extracted xylan depend on the type of biomass and the pretreatment used (Brienzo et al. 2016). Xylan contains side chains such as acetyl group and arabinofuranosyl groups, which leads to the synthesis of branched XOS (de Freitas et al. 2019). Extracted xylan is hydrolyzed by endo β-1,4-xylanase to produce the XOS (Akpinar et al. 2010). The quantity of monomeric units, as well as the degree of polymerization of XOS, depends on the source of extracted xylan, the type of pretreatment, and the duration of enzymatic hydrolysis. The endoxylanases from GH10 family are less xylan specific as compared with those from GH11 family (Moreira 2016). XOS has numerous applications in nutraceutical, pharmaceutical, and biomedical fields. The XOS can be used as partial substitute for other sugars in the pharmaceutical and food industries. XOS possesses antioxidant properties and stimulates the immune system (Samanta et al. 2013). XOS also enhances the long chain fatty acid production, thereby reducing the serum triglycerides and cholesterol level (Samanta et al. 2015).

XOS stimulates the selective growth of gut microflora owing to its prebiotic properties (Sharma et al. 2020b).

## 14.3.2 Xylan Derivatives

### 14.3.2.1 Xylan Ester

The esterification of xylan can be achieved by derivatization reactions in a homogeneous *N*,*N*-dimethylformamide (DMF)/LiCl system (Petzold-Welcke et al. 2014). In this system, satisfactory substitutions can be achieved along with the xylan backbone with a shorter chain. The reaction in heterogeneous or gel-like phase reduces the degree of substitution in xylan extracted from biomass. Xylan esters have biomedical applications owing to their heparin-like property of preventing blood coagulation (Pawar et al. 2008).

### 14.3.2.2 Sulfated Xylan

The extraction of xylan from different agriculture wastes is a new trend that involves lower cost and can be used for production of various promising value-added derivatives (Wang et al. 2007). The sulfation of extracted xylan was carried out either in a homogeneous or heterogeneous system based on the partially or actively suspended xylan in an aqueous solution (dos Santos et al. 2016). The sulfation reaction mainly occurred at free C-2, C-3, and C-6 hydroxyl group of each anhydrous glucose unit present in the xylan side chain. The modification in xylan by sulfation is a simple and feasible strategy to achieve a wide range of biological activities (Ragab et al. 2018).

### 14.3.2.3 Xylan-Based Other Biorefinery Products

The products such as xylitol, ethanol, 2,3-butanediol (2,3-BD), and butanol are also produced from xylan. Xylitol, the 5 carbon sugar alcohol is used as a substitute in dietary foods, especially in the insulin deficiency diabetics (Chen et al. 2010). Xylitol is also used in pharmaceutical as anticancer agent and food industries, for its low calorific value, high sweetening and microbial growth inhibiting properties (Ur-Rehman et al. 2015). 2,3-BD is an alternative to traditional ethanol and has extensive applications in chemical industries as a growth stimulator and pesticide in plants (Li et al. 2016). It is also used in cosmetic and pharmaceutical industries as antiseptics and anti-inflammatory agent (Song et al. 2019). Organic acid such as lactic acid produced from xylan also has applications in the pharmaceutical, food, and chemical industries (Li et al. 2016).

## 14.4 Biomedical and Pharmaceutical Applications of Xylan Derivatives

The pharmacologically active polysaccharides are found in the plant cell walls. The progress in the pharmaceutical and biomedical fields has raised the demand for precursors to be used for specific applications. To fulfill these requirements, plant polysaccharides can be the potential and cheap source of feedstock. The xylan derivatives such as XOS, sulfated xylan, and esterified xylan have received attention owing to their wide applications in cosmetics, food, biomedical and pharmaceuticals (Zhang et al. 2005; Coviello et al. 2007). The sulfated xylan derived from xylan extracted from rice straw and husk showed promising anticoagulation and fibrinolytic activities in the albino rat (Ragab et al. 2018). Arabinoglucuronoxylans isolated from various herbal plants showed immune-stimulating properties (Fadel et al. 2018). Linear or debranched xylan are mainly used as surface modifiers for cellulosic materials (Bosmans et al. 2014) or to make hydrogels as drug delivery systems (Chimphango et al. 2012). The applications of xylan-based biorefinery products are listed in Table 14.2.

From sulfation of beechwood xylan, an FDA-approved oral medicine pentosane polysulfate has been produced, which is known for its anticancer, anticoagulant, and anti-inflammatory effects and also for lowering the triglyceride and cholesterol levels in human (Schuchman et al. 2013). The XOS produced from xylan by enzymatic hydrolysis can be used as prebiotics, which selectively enhances the growth of beneficial gut microflora (Samanta et al. 2015). Other health benefits of XOS are enhancement of mineral absorption in the large intestine, immune-stimulation and reduction of pro-carcinogenic enzymes in the gastrointestinal tract,

**Table 14.2** Xylan-based biorefinery products and their applications

| Xylan derivatives | Applications | Reference |
|---|---|---|
| Sulfated xylan | Anti-herpes simplex virus activity | Mandal et al. (2010) |
| Xylan microparticle | Drug delivery system | da Silva et al. (2012) |
| Xylooligosaccharides | • Stimulate selective growth of gut microflora | Samanta et al. (2015) |
| | • Antioxidant property | |
| | • Stimulate immune system | |
| | • Enhance long chain fatty acid production | |
| | • Reduce serum triglycerides and cholesterol level | |
| Xylan-based biofilms | Controlled drug release or improved medical imaging | Ma et al. (2017) |
| Hydrogel | • Construct three-dimensional regenerative tissue | Chai et al. (2017) |
| | • Screening of anticancer drugs | |
| | • Self-healing gel | |
| | • Drug delivery system | |
| Esterified xylan | Enhancing the flexibility and hydrophobicity of hemicellulose films | Zhao et al. (2020) |

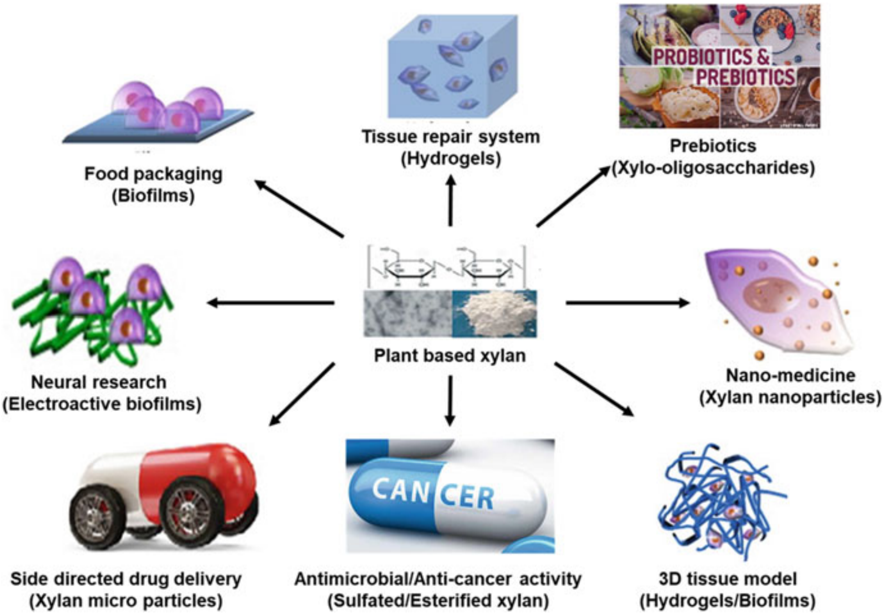

**Fig. 14.2** Biomedical and pharmaceutical applications of xylan and their derivatives

and reduction in cholesterol and blood glucose level (Vazquez et al. 2000; Samanta et al. 2015). Japan has been incorporating the XOS into prebiotic drinks (Vazquez et al. 2000). The biomedical and pharmaceutical applications of xylan are shown in Fig. 14.2.

### 14.4.1 Xylan-Based Drug Delivery Systems

#### 14.4.1.1 Xylan-Based Films for Drug Delivery

The structure of polymeric films can create a useful drug delivery system and this property has received significant attention from pharmaceutical industries (Bassi and Kaur 2017). The low environmental impact, availability, renewability, and simplified end-of-life disposal are the advantages of these biopolymers (Saxena et al. 2011). In the last decade, a new concept has emerged about the utilization of biodegradable xylan and other polymers for the synthesis of polymeric films. Xylan can produce a biofilm on its own due to the properties such as the presence of branches, polymer chain size, low water solubility, low molecular weight, and high glass transition temperature (Jin et al. 2019). The xylan-based biofilms are dependent on the type and the degree of substitution, polymerization, and extraction method used (Escalante et al. 2012; Lucena et al. 2017). Lignin containing xylan-based biofilms can be formed without the addition of a plasticizer (Goksu et al. 2007). In the xylan extracted from cotton stalk and birchwood, at least 1% (w/w) lignin is required in the xylan to form a biofilm (Goksu et al. 2007). The lignin might be acting as a reinforcing agent for xylan film (Jin et al. 2019). The addition of salts in biofilms decreases their tensile strength (Mikkonen et al. 2009).

### 14.4.2 Xylan-Based Hydrogels for Drug Delivery

The three-dimensional hydrophilic macromolecular network of the polymer can absorb and retain a considerable amount of aqueous liquid and form a hydrogel. It is widely used in agriculture, biomedical and environmental applications. The hydrogel has a high degree of flexibility, mechanical properties, and water holding capacity and therefore can be used in diverse applications. The conducting property of hydrogel has received immense attention in recent years. These are polymeric co-networks that bind inherently with the highly hydrated hydrogels and have reported applications in cell activity stimulation (Liu et al. 2018), cell repair (Fu 2018), and nerve tissue re- and de-generation (Xu et al. 2016; Han et al. 2018) even in electrical stimulation absence (Wen et al. 2020). Xylan-based hydrogels have been used in drug delivery (Gao et al. 2016), the cell-matrix (Venugopal et al. 2013), and tissue engineering (Wallenius et al. 2015). Xylan-based hydrogels have gathered substantial attention owing to their biocompatibility, biodegradability, and nontoxic properties (Venugopal et al. 2013; Park et al. 2015). Xylan biopolymer cannot be digested in the intestine and stomach but can be digested by the human colonic microflora (Wang et al. 2016). Due to this reason, xylan is used to prepare a drug delivery system that has the aim of achieving the controlled drug release in the colon region. The induction of physical or chemical cross-linking reactions is mainly used to prepare these drug delivery systems. A caffeine loaded xylan-based hydrogel was prepared by the chemical cross-linking catalyzers such as horseradish peroxidase and hydrogen peroxidase (Iravani et al. 2011). This drug delivery system followed the Fickain diffusion process in both 0.1 M HCl and distilled water (Iravani et al. 2011). For the controlled drug delivery system, a xylan-based hydrogel from wheat straw was reported as a novel carrier (Sun et al. 2013). The xylan polymer was combined with acrylic acid using *N*,*N*-methylene bis-acrylamide as a cross-linking agent and the model drugs such as acetylsalicylic acid and theophylline were used. The pH dependence of drug release of the hydrogel was revealed in a study with different pH solutions (pH 1.5, 7.4, and 10) (Sun et al. 2013). At pH 7.4, a greater amount of drug release was found and a sustained release was maintained for 5–6 h. Similar to the production of biofilms, xylan-based hydrogels from polymeric blends have been developed. The most common blend prepared from xylan-based hydrogels is the mixture of xylan with acrylic derivatives. Gao et al. (2016) prepared a hydrogel with acetylsalicylic acid loading at the different polymer cross-linking agent (*N*,*N*-methylene bis-acrylamide) ratios. They also concluded that the encapsulation efficiency of the drug increases when the amount of acrylic acid increases and this decreases the swelling ability of the hydrogel. The methacrylate acid blended xylan has also been developed and studied previously (Sun et al. 2015). Xylan also can be blended with natural polymers (e.g., chitosan) to develop hydrogels and these hydrogels have a comparatively good swelling capacity (da Costa Urtiga et al. 2020). No alteration in the mitochondrial activity of 3T3 fibroblasts was found in the modified xylan-based hydrogels (Gao et al. 2016). Modification of xylan with the synthetic polymers might be riskier to use clinically. The cytotoxicity of synthetic polymers depends on their molecular mass, electric charge, branching, concentration, and exposure time duration (Mellati et al. 2016; Jeong et al. 2017). However, the polymers with cations (polycations) on their surface are more toxic than the neutral and anionic polymers (Jeong et al. 2017).

### 14.4.3 Xylan-Based Microparticles and Nanoparticles for Drug Delivery

The first report on the use of xylan for producing nano- and microparticles was from corncob xylan (Garcia et al. 2001). These micro- and nanoparticles were produced by the coacervation process by adding HCl or acetic acid solution into the alkaline xylan solution. The size of the xylan particles was dependent on the concentration of xylan (da Silva et al. 2012). However, the micro- and nanoparticles produced from xylan did not show stability and after few days they formed flocculates in the solution. The addition of surfactant improved the stability of the micro- and nanoparticles but caused toxicity to the cell (da Costa Urtiga et al. 2020). As per the previous reports, the less toxic reagents should be used for the formulation of micro- and nanoparticles. These formed particles should be quantified to meet the limitation laid by the drug regulatory agencies (Araújo et al. 2015). Interfacial cross-linking polymerization method was used for the production of xylan microcapsules (da Costa Urtiga et al. 2020). The cytotoxicity study of xylan and xylan-based microparticles produced by an interfacial cross-linking method using terephthaloyl chloride was evaluated (Marcelino et al. 2015). In a previously studied MTT (3-(4,5-dimethylthioazol-2-yl)-2,5-diphenyltetrazolium bromide) assay by using the human cervical adenocarcinoma cells (HeLa), xylan showed biocompatibility in the concentration range from 4.1 to 12.4 mg/mL. The xylan microparticles cytotoxicity was attributed to the presence of the non-reacting radicals produced from the terephthaloyl chloride (da Costa Urtiga et al. 2020). To overcome the cell toxicity, a nontoxic cross-linking agent such as sodium tri-metaphosphate was used from the production of xylan microparticles (Cartaxo da Costa Urtiga et al. 2017). Xylan microparticle based nonspecific drug delivery system is shown in Fig. 14.3.

The toxic effect of xylan biomaterials on cells is one of the most important issues that have to be considered during pharmaceutical product development. In vitro toxicity is correlated with cell death, cell adhesion, cell proliferation, and cell morphology. Because of that, loss of cell viability could be the consequence of a toxic xylan compound (da Silva et al. 2012). Xylan is especially useful in the production of colon-specific drug carriers (Oliveira et al. 2010). The abundance of xylan in nature, its biodegradability and biocompatibility make it more beneficial to the industry as well as to the environment.

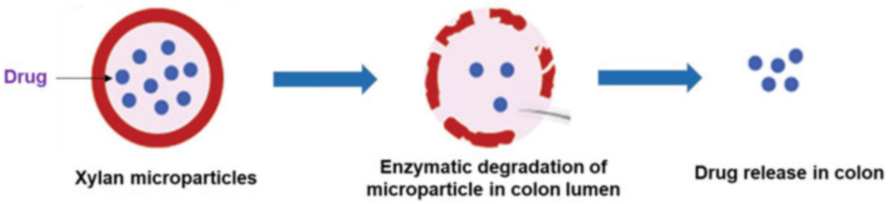

**Fig. 14.3** Xylan microparticle based nonspecific drug delivery system

## 14.5 Conclusions

Over the last few decades, hemicelluloses have been extensively studied for potential pharmaceutical and biomedical purposes, mainly because of their biocompatibility and sustainable source of extraction. Numerous efforts are centered around the xylan extraction process, structural modification and their applications, particularly in biomedical and pharmaceutical fields. Additionally, xylan can be also used for the production of other derivatives such as hydrogel and biofilms for food and cosmetics industries. However, some of the problems related to biomedical and pharmaceutical applications are still unresolved such as a wide variety of composition, the physico-chemical limitation in biofilms formation, the limited clinical studies, and well-established protocols to evaluate the xylan-based systems. To overcome these challenges, further exploration is required for establishing and validating the xylan extraction methodologies, chemical modification approaches and improving its biomedical applications.

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# Hemicellulose-Based Delivery Systems: Focus on Pharmaceutical and Biomedical Applications

# 15

Payal H. Patil, Chandrakantsing V. Pardeshi, Hitendra S. Mahajan, and Sanjay J. Surana

## Abstract

Hemicellulose is the second most prevalent, renewable, non-toxic, and biodegradable hetero-polysaccharide after cellulose in plants consisting of different saccharide units. Hemicellulose's versatile physical and chemical properties make it a promising source for applications in pharmaceutical and biomedicine fields. Hemicellulose and derivatives find wide pharmaceutical applications in the preparation of hydrogels, microspheres, films, nanocomposites, microgels, bionanofibers, and so on. Biomedical applications include wound healing and tissue engineering. This chapter explains the fundamental aspects relevant to hemicelluloses, viz. structure, sources, properties, and their biodegradability and/or biocompatibility. The authors also present the potential of stimuli-responsive hemicellulose-based hydrogels for pharmaceutical applications. The major aim of this chapter is to summarize the research-based investigations on fabrication, and applications of hemicellulose-based formulations and their future perspectives.

## Keywords

Hemicellulose · Derivatives · Drug delivery · Biocompatibility · Biodegradability · Biopolymers

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M. Brienzo (ed.), *Hemicellulose Biorefinery: A Sustainable Solution for Value Addition to Bio-Based Products and Bioenergy*, Clean Energy Production Technologies, https://doi.org/10.1007/978-981-16-3682-0_15

## 15.1 Introduction

Renewable resources of materials are indeed required in the future decades to meet the needs of the society, as the world is becoming increasingly mindful of the limited availability of fossil fuels. To address this issue, lignocellulosic biomass from grasses, cereals, trees, and some other plant sources seems to have become the prime focus of several biorefineries (Ragauskas et al. 2006). Plant materials mainly consist of three basic kinds of biopolymer: hemicellulose, cellulose, and lignin, among which cellulose and lignin have gained worldwide prominence in biomedical applications. Hemicelluloses are, after cellulose, the second most available renewable type of polymer that is obtained from plants. Given their multiple perceived advantages, such as non-toxicity, biocompatibility, biodegradability, and anti-cancer effect, greater interest has been focused on the production and utilization of hemicellulosic materials (Ebringerová et al. 2005; Karaaslan et al. 2011; Oliveira et al. 2010). Although cellulose seems to have a distinct structure, a range of non-crystalline hexose and pentose sugars are defined under the term hemicellulose. Hemicellulose is historically known as the alkali-soluble material after removing the pectic substances from the walls of plant cells (Sun et al. 2003). It is possible to identify four major classes of hemicelluloses by their primary structure: xylans, mannans, mixed β-glucans, and xyloglucans (Ebringerová and Thomas 2005). Schulze originally coined the term hemicellulose in the year 1890 to describe polysaccharides extractable from higher plants by aqueous alkaline solutions as contrasted with cellulose (Ebringerová and Thomas 2005). These exist in close connection with cellulose and lignin and relate to the stiffness of lignified tissue plant cell walls. Hemicelluloses make up nearly 20–30% of the total annual and perennial plant mass and also have a heterogeneous proportion of different sugar units, based on the type of plant and the process of extraction (Belgacem and Gandini 2008).

In this chapter, we discuss the pharmaceutical and biomedical applications of hemicellulose-based formulations. As a framework, we start by introducing the hemicellulose, their structure and sources, biodegradability and biocompatibility characteristics, and gelation mechanism. Then, the major focus of the chapter is on the applications of hemicellulose-based formulations for the therapy of variety of disorders. The researchers, academicians, and industrialists working on the hemicellulose-based formulations will certainly be benefited from this chapter entry.

## 15.2 Structure

In several instances, xylans are made of a β (1→4)-D-xylopyranose (Fig. 15.1) framework containing 2- or 3-position side groups. In certain seaweeds, non-branched homoxylans exist with β (1→3, 1→4) or β (1→3) glycosidic linkages. Heteroxylans comprise glucuronoxylans and arabinoxylans along with structures occasionally simply called as heteroxylans with more complex substitution patterns. Glucuronoxylans have a 2-position side chain of either α-D-glucuronic acid or its

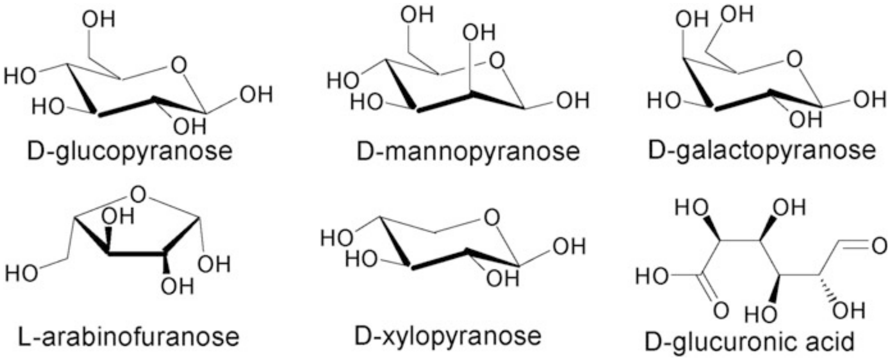

**Fig. 15.1** Main constituents of hemicellulose (Hansen and Plackett 2008)

4-*O*-methyl derivative, whereas arabinoxylans are substituted with α-L-arabinofuranosyl residues at position 2 and/or 3 (Ebringerová and Thomas 2005; Wikipedia n.d.).

There are two kinds of mannans, namely galactomannans composed of β (1→4) connected D-mannopyranoses and glucomannans composed of D-mannopyranose and D-glucopyranose connected to β (1→4). In the 6-position mannose framework, both forms of mannoglycans have different degrees of branching with D-galactopyranose residues. β-glucans also have a backbone of D-glucopyranose containing mixed bonds (1→3, 1→4) in varying proportions and can form extremely viscous solutions and gels (Ebringerová and Thomas 2005). Xyloglucans do have a framework of D-glycopyranose residues connected to β (1→4) with a D-xylopyranose distribution at position 6. The arrangement of the side groups separates the xyloglucans into two major categories: including one with two units of xylopyranose followed by two units of glucopyranose (XXGG) and one with three units of xylopyranose followed by one unit of glucopyranose (XXXG). Besides a variety of side chains occur on xyloglucans, particularly α-L-arabinofuranose, which makes it particularly difficult to classify this category of hemicelluloses (Table 15.1) (Hansen and Plackett 2008; Wikipedia n.d.).

## 15.3 Sources

There have been substantial studies on such hemicelluloses. An example is konjac glucomannan, derived from the Amorphophallus konjac tuber. One such hemicellulose has already been used extensively for several years (Ebringerová 2005), but due to the gel- and film-forming characteristics, along with biocompatibility and biodegradability of such a polysaccharide, research has increasingly intensified. Such properties have been used in many applications in areas of delivery of drugs, cell therapy, entrapment, and emulsification (Zhang et al. 2005).

**Table 15.1** Major components of hemicellulose (Structure and properties of hemicellulose)

| Hemicellulose | Occurrence | Amount (% of wood) | Composition | | | Solubility | $\overline{\mathrm{DP}}$ |
|---|---|---|---|---|---|---|---|
| | | | Units | Molar ratios | Linkage | | |
| Galactoglucomannan | Softwood | 5–8 | β-D-Manp | 3 | 1→4 | Alkali, water[a] | 100 |
| | | | β-D-Glcp | 1 | 1→4 | | |
| | | | α-D-Galp | 1 | 1→6 | | |
| | | | Acetyl | 1 | | | |
| (Galacto)glucomannan | Softwood | 10–15 | β-D-Manp | 4 | 1→4 | Alkali, borate | 100 |
| | | | β-D-Glcp | 1 | 1→4 | | |
| | | | α-D-Galp | 0.1 | 1→6 | | |
| | | | Acetyl | 1 | | | |
| Arabinoglucuronoxylan | Softwood | 7–10 | β-D-Xylp | 10 | 1→4 | Alkali, dimethylsulfoxide[a], water[a] | 100 |
| | | | 4-*O*-Me-α-D-GlcpA | 2 | 1→2 | | |
| | | | A-L-Araf | 1.3 | 1→3 | | |
| Arabinogalactan | Larchwood | 5–35 | β-D-Galp | 6 | 1→3, 1→6 | Water | 200 |
| | | | A-L-Araf | 2/3 | 1→6 | | |
| | | | β-D-Arap | 1/3 | 1→3 | | |
| | | | β-D-GlcpA | Little | 1→6 | | |
| Glucuronoxylan | Hardwood | 15–30 | β-D-Xylp | 10 | 1→4 | Alkali, dimethylsulfoxide[a] | 200 |
| | | | 5-*O*-Me-α-D-GlcpA | 1 | 1→2 | | |
| | | | Acetyl | 7 | | | |
| Glucomannan | Hardwood | 2–5 | β-D-Manp | 1–2 | 1→4 | Alkali, borate | 200 |
| | | | β-D-Glcp | 1 | 1→4 | | |

[a] Represents a partial solubility

One more example of hemicellulose utilized widely is tamarind seed xyloglucan, which is often used in the delivery of drugs. Usage of this and other polysaccharides in the release of formulations for hydrogels seems to be the subject of a new study reported by Coviello et al. (2007). Hemicellulose is linked to cellulose and lignin within the plant cell wall and extensive separation processes are needed to isolate such materials from the raw material of plants. Hemicellulose composition varies according to different feedstocks, as well as between sources, based on several factors such as the stage of origin and stage of development. An example is the latest research of four varieties of rice showing significant differences in the key components (Edlund and Albertsson 2008) xylose (17–40%), glucose (36–55%), and arabinose (5–23%), amongst the diverse cultivators (Hansen and Plackett 2008). Several techniques are utilized for extracting hemicelluloses through plant sources, namely alkali, dimethyl sulfoxide, or methanol/water extraction, and steam or microwave processing. The content of the obtained hemicellulose can be largely dependent on the method of isolation and may occur, for example, deacetylation, degradation, and lignin contamination. The research reported by Sun et al. (2005) shows the composition dependence on the isolation method since the pre-treatment of wheat straw samples using different organic solvents before extraction culminated in significantly different hemicellulosic products.

## 15.4 Biodegradability and Biocompatibility of Hemicelluloses

Because of their renewability, biodegradability, biocompatibility, and excellent oxygen barrier properties, hemicelluloses are commonly used to prepare gel formulations. The biocompatibility study demonstrated that the hydrogels based on hemicellulose showed no cell toxicity and allowed cell growth (Cao et al. 2014). It is envisaged that perhaps the degradation mechanisms on hemicellulose take place in two ways. Firstly, the degradation by the exoglycosidases accompanies that of the hemicellulases (i.e., xylanase, galactanase, and B-mannanase), eliminating the functional groups of the side chain, thus “opening” or displaying the backbone glycan chain. In this way, the hemicellulases could more effectively target the glycan chain, as a steric hindrance by the residues of the side chain decreases. Additionally, endohemicellulases strike unbranched or comparatively slightly branched regions of the glycan chain with substituents. Endohemicellulase activities produce a range of mixed-constitution oligosaccharides, which is further degraded by both exoglycosidases and endohemicellulases.

However, two exceptions to the envisaged modes of attack are the behavior of the debranching endoxylanases and exohemicellulases. It has been shown that the debranching endoxylanases can also cleave L-arabinose units from arabinoxylans and arabinoglucuronoxylans, and hence wouldn’t need the aid of the α-L-arabinosidases to help open the xylan chain. Concerning the exohemicellulases, one might anticipate from certain enzymes modifying hemicelluloses with minimal hydrolysis, as their activities are halted when branch-point substituents are reached.

Such constraints will therefore rely on whether or not the hemicellulase attack was followed by the exoglycosidases action.

The exoglycosidases attack the low molecular weight oligosaccharides produced by the action of endohemicellulases and are also capable of hydrolyzing the branch points on the hemicellulose backbone chain. Thus, the α-L-arabinosidases and α-D-glucuronidases remove the L-arabinose and D-glucuronic acid substituents from arabinoglucuronoxylans and glucuronoxylans; α-D-galactosidases cleave the α-D-galactose residues from galacto-glucomannans, and the L-arabinosidases and β-D-galactosidases are responsible for the hydrolysis of the L-arabinose and D-galactose appendages from arabinogalactans. The oligosaccharides resulting from invasion by the hemicellulases and exoglycosidases on hemicellulose would be further deteriorated by the activities of another group of exoglycosidases. It included β-D-xylosidases, β-D-mannosidases, and β-D-galactosidases, that, specifically, assault low MW 1,4-β-D-xylosides, 1,4-β-D-mannosides, and 1,4-β-D- and 1,3-β-D-galactosides (Dekker 1985).

## 15.5 Gelation Mechanism of Hemicelluloses

As a physical procedure, the freeze-thaw method (Fig. 15.2) creates stable hydrogels, which are physically interlinked by the existence of a crystalline structure. Materials prepared by the freeze-thaw method have shown improved mechanical properties when compared to their non-toxic nature, especially for biomedical applications. The freeze-thaw method can produce hydrogels with excellent mechanical properties and elevated elasticity, which are ideal for artificial tissue and other biomaterial implementations (Tamura et al. 1986; Yon et al. 1994).

## 15.6 Applications

### 15.6.1 Pharmaceutical Applications

To tackle the challenges of traditional wound dressings, new wound dressings (film wafers, hydrogels, and sponges) are intended. The development and implementation of such dressings have also been carefully examined (Naseri-Nosar and Ziora 2018; Simões et al. 2018), where it is being stressed that perhaps the dressing products should be biocompatible, absorb exudate, permit the transmission of water vapor (WVTR) and have antimicrobial properties (Farzamfar et al. 2018; Naseri-Nosar and Ziora 2018).

#### 15.6.1.1 Hydrogels

They are complex 3D hydrophilic structures that swell in an aqueous medium and are chemically or physically cross-connected (Anseth et al. 1996). The classification of hydrogels is given in Fig. 15.3. The existence of hydrophilic groups in polymers, like amine (-$NH_2$), carboxylic (-COOH), sulfate (-$SO_3H$) groups, offers good water

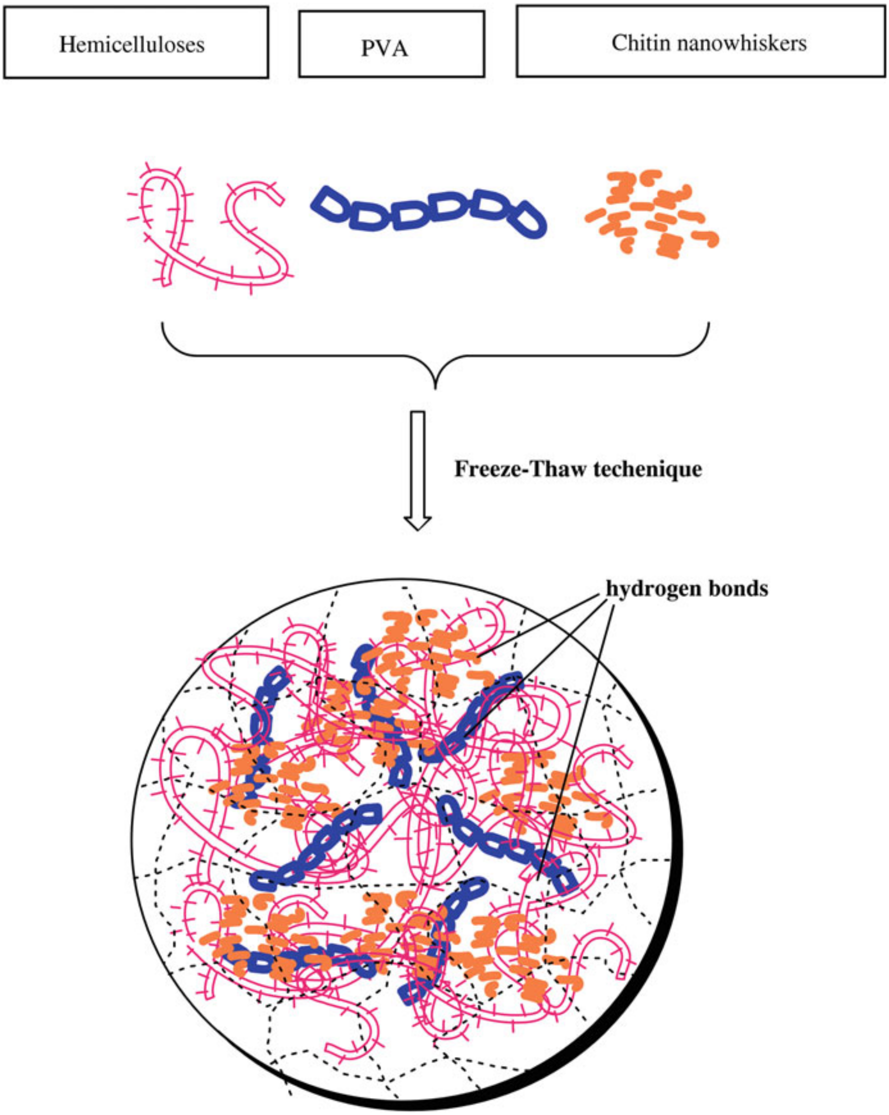

**Fig. 15.2** Gelation mechanism of hemicellulose, PVA, and chitin nanowhiskers in the freeze-thaw process (Guan et al. 2014)

locking potential for hydrogels as well as the rate of water imbibition of these three-dimensional cross-linked polymers can vary from one hundred to a few thousand folds their weight (Gupta et al. 2002; Mathew et al. 2018). They have numerous uses in biomedical, agricultural, medicinal, and daily care applications, such as tissue engineering, contact lenses, wound dressing, medication delivery as well as a super-absorbent agent, with high water absorption, retention properties, and strong

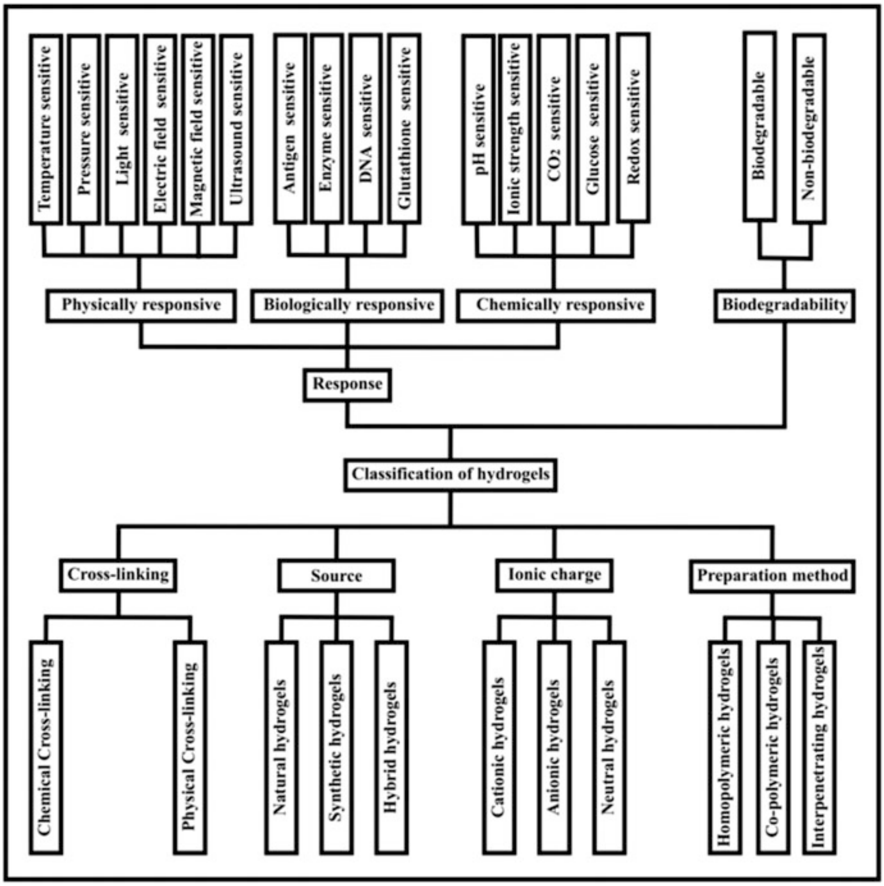

**Fig. 15.3** Classification of hydrogels (Rizwan et al. 2017)

biocompatibility, special physical properties, permeability and tissue-mimicking quality (Smith et al. 2010; Vermonden et al. 2012). Due to the existence of solvent molecules during the hydrogel-forming process, the majority of polymeric hydrogels are fragile and vulnerable to rupture when treated in a swollen state, exhibiting characteristics such as low break strain and weak extensibility (Cui et al. 2012; Isobe et al. 2011). Hence the achievement of high-mechanical strength hydrogels is essential for their effectiveness if used in areas where durability is necessary. Owing to the nature of such chemical, covalent, ionic, or physical cross-links, hydrogels are made insoluble (Karaaslan et al. 2011; Mc Gann et al. 2009).

Unique structural similarity with the extracellular matrix (ECM) and because of their ability to sustain a humid environment, that is important for the healing process, hydrogels are favored as nanostructures for tissue engineering (Lin et al. 2011; Rimmer 2011). The products based on bacterial cellulose, such as XCell®, Bioprocess®, Biofill®, c X®, and Dermafill, are already marketed for wound healing dressing (Petersen and Gatenholm 2011; Portal et al. 2009). Hemicelluloses provide numerous beneficial biological properties from multiple sources, like antioxidant, antitumor, and immunomodulatory action, and have been designed for tissue engineering, drug delivery, wound care, cancer prevention, detection, and therapy applications (Liu et al. 2015). However, the mechanism about how hemicellulose integration into nanocellulose scaffolds controls the mechanical properties of hydrogels and thus has not been investigated systematically for the cellular response through cell culture.

##### 15.6.1.1.1 Hydrogels Using Chemically Modified Hemicellulose

On every repeating unit, hemicellulose has active hydroxyl groups that are the reactive sites for chemical functionalization. The introduction of new functional groups on hemicellulose to make it inter-or intra-molecularly cross-linkable is one method for preparing hemicellulose-based hydrogels (Li and Pan 2010).

##### 15.6.1.1.2 Hemicellulose-Containing Interpenetrating Network (IPN) Hydrogels

In particular, the mechanical strength of hydrogels dependent on polysaccharides is weak (Vieira et al. 2008). Mechanical characteristics have also been enhanced without any impairment of their absorption capacity. One of its techniques to boost the material characteristics of hydrogels is the development of IPN or semi-IPN hydrogel (Jagur-Grodzinski 2010; Tang et al. 2009). One polymer was cross-linked in the hydrogels with IPN/semi-IPN structure, in the presence of another cross-linked/non-cross-linked polymer. Hydrogen chains, crystallites, and the ionic and hydrophobic associations in between two polymers influence the hydrogel characteristics (Moon and Kim 2010).

Due to their sensitivity to external stimuli, like pH, ionic strength, solvent composition, temperature, and electric and magnetic fields, intelligent hydrogels have indeed been extensively studied recently (Qiu and Park 2001). These stimuli can induce reversible swelling and de-swelling of hydrogels (Huang et al. 2019a, b). Hydrogels may be widely used in biomedical fields due to its excellent properties, particularly biological tissue engineering scaffolds (Hoffman 2012), biosensors, immobilized carriers for the encapsulation of living cells (Sefton et al. 2000), barrier materials for the regulation of biological adhesions (Bennett et al. 2003) and regulated drug delivery systems (Lin and Metters 2006; Qiu and Park 2001).

###### Temperature-Responsive Hydrogels

These are the hydrogels that gels at physiological temperatures and they offers excellent spatial as well as temporal power to the delivery system. They are widely used in drug delivery, tissue engineering, imaging, and wound care (Huang et al. 2019a, b). They are the finest polymeric approach researched since the temperature is inherently variable and simple to regulate. The volume (swelling/de-swelling) and transmission of thermosensitive hydrogels should render it to respond intelligently with the temperature change. They usually contain both hydrophobic and hydrophilic parts in frameworks, and the phenomenon of thermal change is obtained from

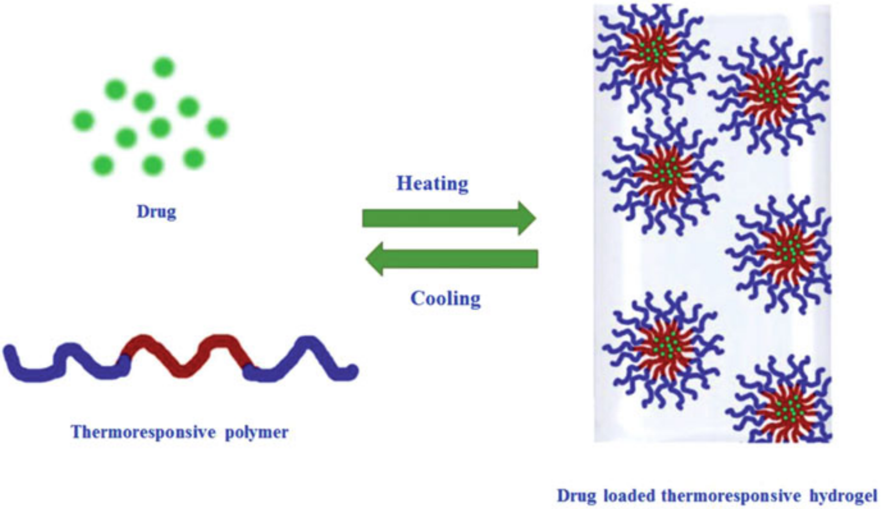

**Fig. 15.4** Mechanism of formation of thermoresponsive hydrogel (Chatterjee et al. 2018)

the precarious balance of the monomer's hydrophilic or hydrophobic parts (Qiu and Park 2001; Xue et al. 2002). The temperature varies the interaction of the polymer with water molecules within hydrophilic and hydrophobic parts, so that the solubility of the cross-linked network changes, triggering the transformation of the sol-gel process (Fig. 15.4) (Bajpai et al. 2008). Although the gel state is non-flowing and retains its integrity, the sol state is characterized as a flowing fluid. The macroscopic soluble state of the cross-linking framework in an aqueous solution is determined by altering the equilibrium of hydrophilicity and hydrophobicity (Jeong et al. 2012). It depends on the thermosensitive groups; microscopic mechanisms can attain the gelling property of thermosensitive hydrogels. They show the solution and solid segregation at either the lower critical solution temperature (LCST) or the upper critical solution temperature (UCST) (Ishida et al. 2012; Schild and Tirrell 1990). Under the LCST, the polymer dissolves as it keeps shrinking, hydrophobic, and insoluble at the LCST temperature, resulting in gelation. In comparison, there is a UCST in the hydrogel produced on the cooling of the polymer solution. More precisely, a phase shift from a soluble state (discrete coil) to an insoluble state (collapse or micelle form) is demonstrated by the polymer in the solution near the critical temperature. By changing the hydrophilic to hydrophobic ratio, the inherent LCST can be set (Qiu and Park 2001).

Since the controllable release of the biologically active drug is susceptible to temperature changes, thermosensitive hydrogels have also been broadly accepted. As a delivery mechanism, thermosensitive gels have several benefits. Except for conventional hydrogels, the temperature-sensitive properties give the hydrogel injectability for local administration to be inserted surgically, which can prevent the first-pass metabolism. The temperature-sensitive gel reacts to temperature, and the transformation of the temperature-induced sol-gel is safer in the body and more suitable for injectable systems since no cross-linking agent is needed for denaturing. Entrapment in a circulating state facilitates the homogeneous distribution of the drugs in hydrogels, although the drastic change from sol-to-gel at body temperature prevents the drug molecules from initially bursting, thus regulating the release behavior in a controlled way. The flowable state of administration finally bestows the controllability of the hydrogel form (Huang et al. 2019a, b). The drug release mechanisms for hydrogels could be categorized as passive diffusion, hydrogel erosion, and chemical control (Amsden 1998; Canal and Peppas 1989).

While developing a temperature-sensitive gel for biomedical applications, several aspects must be underlined as below: (a) The biocompatibility and biodegradability of gel would be influenced by the choice of temperature-sensitive polymer forms. (b) The porosity of the gel should be modified in conjunction with the drug-loaded, thus controlling the drug release and the maintenance of cellular activity. (c) The mechanical rigidity of the in situ shaped temperature-sensitive hydrogels has a significant effect on its practical implementation. (d) To reduce the initial rapid drug release, the length of the gelling period must be monitored. (e) Suitable temperature-sensitive products like oral, ocular, rectal, vaginal, and parenteral must be chosen as per the administration route to fulfill on-demand therapeutic release in the body (Huang et al. 2019a, b).

A self-healing thermosensitive hydrogel focused on chitosan/b-sodium glycerophosphate and polyethylene glycol (DF-PEG) filled with DOX was developed by Han et al. (2018). Gels were administered into a Heps tumor model in mice to monitor tumor progression by intratumoral injection, demonstrating excellent tumor suppression and relieving DOX cardiotoxicity. A pluronic F127 (PF127) and *N*,*N*,*N*-trimethyl chitosan (TMC) mixed thermosensitive hydrogel loaded with docetaxel (DTX) has been developed by Turabee and coworkers (Turabee et al. 2019) for glioblastoma care. In this gel system, the inclusion of TMC improved the porosity of the gel network and strengthened the mechanical properties of PF127, thus improving the aggregate strength of DTX. For further a month, the thermoresponsive hydrogel approach shows sustained release of DTX and provided a successful in vivo brain tumor therapeutic approach. Centered on the chitosan/hyaluronic acid/b-sodium glycerophosphate method, a doxorubicin (DOX) loaded body temperature sensitivity hydrogel was fabricated (Zhang et al. 2018). The mechanical properties were improved by altering the hyaluronic acid ratio, and the gelation temperature could also be adjusted at the same time. The existence of hyaluronic acid, however, prevented the immediate burst release of DOX from the glycerophosphate chitosan/b-sodium system.

### pH-Responsive Hydrogels

pH-sensitive hydrogels have a rather significant role in advanced smart drug delivery systems. In the context of oral drug delivery, pH-responsive hydrogels attracted extensive interest mostly because the hydrogels could preserve the drug towards acid denaturation and decrease the noxious stimulation of drugs on the stomach, but mostly because they may extend the retention time of drugs and reduce dosing

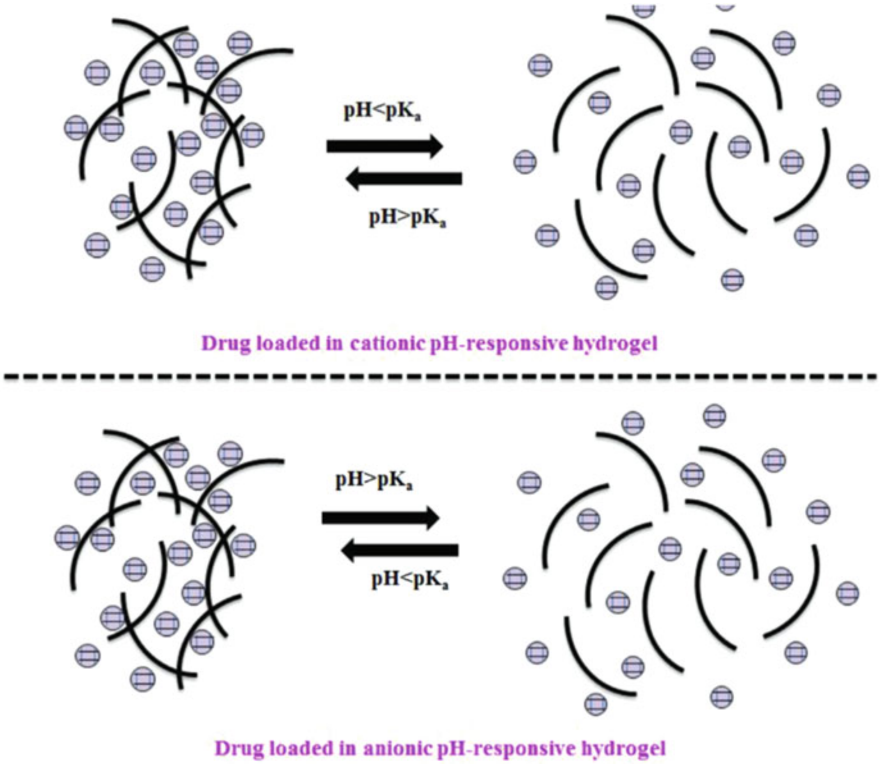

**Fig. 15.5** Mechanism of formation of pH-responsive hydrogel (Chatterjee et al. 2018)

frequency (Qiu and Park 2001). The mechanism of the formation of a pH-sensitive hydrogel is shown in Fig. 15.5. Several natural polysaccharides are often used to formulate hydrogels as a harmless controlled release system for delivery of drugs due to the good biocompatibility and biodegradation of polymeric materials (Coviello et al. 2007; Lindblad et al. 2007). Numerous pH-sensitive hydrogels are being extensively studied and swelling behavior is influenced by the variation in the pH of the environment in the gastrointestinal tract, which ranges between acidic in the stomach to neutral in the intestine (Liu et al. 2010). Hence, they enable the medication to be released at a particular location and are deemed to be excellent targets for the drug delivery system unique to the location. In many biomedical materials comprising MPEG and PLA that are both non-cytotoxic, several products approved by FDA have been used. With excellent permeability, PLA is biodegradable and non-cytotoxic (Habraken et al. 2007; Kalarickal et al. 2007; Li et al. 2005; Sasatsu et al. 2005).

In a study reported by Zheng and coworkers, a type of amphiphilic block copolymer comprising the hydrophilic MPEG and hydrophobic PLA was prepared successfully (Zheng et al. 2010), and the design of the copolymer played a significant role in the characteristics of the pH-sensitive hydrogel. They have also been thoroughly researched as drug delivery systems based on the fact that pH-sensitive hydrogels can efficiently alter their volume in response to specific conditions of different pH values. It has contributed to the fact that external pH can regulate the diffusion and permeation of drug molecules from the hydrogels. IA was selected here to craft a new form of pH-sensitive hydrogel compared to past work because of its two carboxyl groups in one molecule that should attain a reasonable pH-responsive capacity (Wang et al. 2012).

pH-sensitive hydrogels can modify their volume with changes in the pH of the atmosphere in which they are installed. With extreme precision, they are prone to swelling greatly, detecting slight pH shifts of as little as $10^{-5}$ units. Because of their wide measurement range, hydrogels are convincing for pH detection (Riaz et al. 2019; Yong Zhao et al. 2018). Hydrogel-based sensors can be miniaturized and once incorporated in microsystems, are therefore of significant relevance (Riaz et al. 2019). With the identification of micro-scale changes in pH, microcantilevers developed using silicon wafers results show considerable sensitivity (Hendi et al. 2020).

#### Magnetic Field Responsive Hydrogels

Magnetic field responsive hydrogels are indeed a group of materials that, owing to its capability to shift state after magnetic stimulation, has attracted great attention in biomedicine. They are used for the study of drug release, magnetic hyperthermia, and can theoretically be designed for cell mechanobiology as stimuli-responsive substrates. In this context, we suggest a group of magnetic field responsive nanostructured substrates which, once produced by an alternating magnetic field in an aqueous phase, exhibit cyclic swelling and de-swelling phases (Crippa et al. 2017).

Magnetic hydrogels, whereby magnetic nanoparticles are integrated into the hydrogel, might provide an interesting possibility for an applied magnetic field to reversibly alter its mechanical properties. The field-dependence of the appropriate viscosity is well known in the subsequent case of magnetic nanoparticles in a non-polar solvent (“ferrofluid”). Significant field-dependent adjustments in the shear modulus (Wu et al. 2011) and specimen form (Ramanujan and Lao 2006) were recorded in hydrogels with micron-sized magnetic particles (Odenbach 2003). Magnetic nanoparticles have a persistent dipole moment because of their small scale and appear to disperse significantly faster as compared to their micro-sized equivalents.

Magnetic nanoparticles usually exhibit superparamagnetic activity once immersed in a non-polar solvent. Magnetic nanoparticles are likely to exhibit magnetic hysteresis in hydrogels (Monz et al. 2008) because particle rotation in the polymer matrix is seriously impaired and Neel relaxation is slow inside the particles. In a hydrogel doped with magnetic nanoparticles, the fascinating mechanism of self-healing was also reported (Zhang et al. 2012). Thermoreversible ferro hydrogels are now accessible, whereby temperature changes can alter the form and gel strength (Krekhova et al. 2010). Fuhrer and coworkers have documented the powerful but reversible changing shape of a magnetic hydrogel encountered by adjusting the intensity of the external magnetic field (Fuhrer et al. 2009). One such impact can be quite beneficial for not just the artificial muscles, as well as for many other implementations like microfluidic valves (Satarkar et al. 2009), actuators (Snyder et al. 2010), magnetic resonance contrast agents (Kim et al. 2012), hyperthermia (Meenach et al. 2010) or controlled drug delivery (Giani et al. 2012; Paulino et al. 2012). The benefit of such a strategy would be that the hyperthermia (Meenach et al. 2010) or drug delivery be controlled. In biomedical applications, a lack of magnetic material might weaken the hydrogel's properties or indeed contribute to adverse effects. Instead of connecting them somewhere else on the open network strands, the magnetic nanoparticles are used as cross-linking agents (Ilg 2013).

Ren et al. (2006) developed magnetic PLA-PEG particles in another study by combining $Fe_3O_4$ nanoparticles in acetone with poly lactide-co-poly (ethylene glycol) and enabling the suspension to drop into the water, accompanied by acetone evaporation. Liu et al. (2006) fabricated magnetite-loaded cross-linked gelatin hydrogels by combining magnetite nanoparticles into an aqueous phase of gelatin and then cross-linking the resulting mixture with genipin. In a novel work reported by Shamim et al. they developed poly (*N*-isopropyl acrylamide) coated nanomagnetic particles by performing free-radical-induced polymerization of isopropyl acrylamide in an aqueous medium in the presence of uniformly mixed magnetite seed particles (Shamim et al. 2007).

### Photosensitive Hydrogels

Lately, owing to its unique benefits, like localized manipulation, exquisite modulation, and remote and wireless controllability, particularly for cell culture, photosensitive hydrogels have achieved significant attention in the field of clinical and tissue engineering. While conventional polymerization techniques (heat, ionic interaction, and redox) may be used to formulate hydrogels, photopolymerization has attracted the greatest attention in hydrogels (Drury and Mooney 2003; Nguyen and West 2002). Some forms of hydrogels can indeed be developed in situ when exposed to light in the presence of light-sensitive compounds (photoinitiators). Free radicals are produced when UV or visible light interacts with photoinitiators to trigger polymerization and as a result, produce cross-linked hydrogel networks. Photopolymerization provides multiple benefits over traditional polymerization methods, namely rapid reaction kinetics (below several minutes), spatiotemporal command on the polymerization mechanism, and processability at room temperature and physiological conditions (Bryant et al. 2007). A diverse array of photopatterning and stereo lithography-based AMT strategies have been allowed by these kinds of characteristics (Bryant et al. 2007; Liska et al. 2005; Zorlutuna et al. 2011). Implementation of such AMT strategies with hydrogels has allowed more tissue engineering implementations, including in situ cell entrapment and spatiotemporal immobilization of bioactive ligands. We include a material selection guide for water-soluble photoinitiators and hydrogel precursors in this portion, which are key parts for the additive manufacture of 3D hydrogel constructs based on photolithography (Qin et al. 2014).

In contrast to temperature changes, chemical and mechanical strength, for example, it is simple to manipulate individual cell adhesion by low-power irradiation

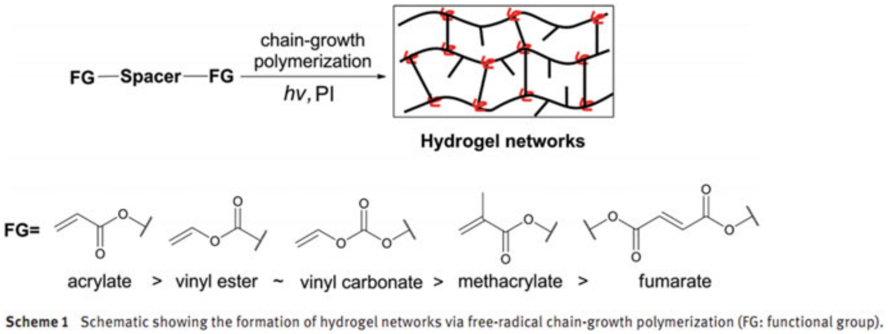

**Fig. 15.6** Mechanism of formation of photosensitive hydrogels (Qin et al. 2014)

(Edahiro et al. 2005) and even selectively kill cells through photoacid generation (Sumaru et al. 2013, 2017) inside the extracellular matrix (ECM) focused on the photosensitive hydrogel. The efficiency of a photo-responsive ECM or scaffold is tightly correlated to the photosensitive hydrogel's stimulus-responsive electrochemical activity that impacts biological activity. For example, a few of the ECM's properties, like water content, hydrophobicity, and mechanical strength, affect cell adhesion (Schmidt et al. 2010), which may differ owing to the photochemical reaction inside the hydrogel. Cell growth, however, largely depends on the temperature, pH, and salt level of the climate. For instance, glycosaminoglycans (GAGs) are always used via their sulfation trends to monitor various growth factors in the scaffold that are heavily influenced by electrostatic interaction and the pH environment inside the microenvironment (Zimmermann et al. 2012).

Also, to track cell behavior inside the ECM, certain observable responses such as electrical impedance or conductivity could be used (Xiao and Luong 2010). Therefore, to enhance the photomonitoring system of photo-responsive ECMs and perhaps other bioelectronics, a self-feedback system can be built for when electrical response signal estimation becomes usable. Towards this point, for more investigation of their prospective use in the biomedical field, it is important to understand the basic response of photosensitive hydrogels subjected to several coupled stimuli, particularly electrical response. The mechanism of the formation of the photosensitive hydrogel is shown in Fig. 15.6. A thorough study of literature shows that photosensitive hydrogels, such as spiropyran (Sugiura et al. 2007), metal nanoparticles (Hauser et al. 2015), chlorophyllin (Suzuki 1994), and photoacid generators (Satoh et al. 2015), have often been synthesized by integrating photo-sensitive groups (PSGs) into the thermoresponsive polymer *N*-isopropyl acrylamide (pNIPAAm).

### Electric-Responsive Hydrogels

Electro-responsive hydrogels recently gained great attention since they are capable of transforming electrical energy into mechanical energy and need less driving voltages (Hines et al. 2017). Polyelectrolytes bearing cations (e.g., chitosan) or anions (e.g., polyacrylic acid) on their structure are usually electric-responsive

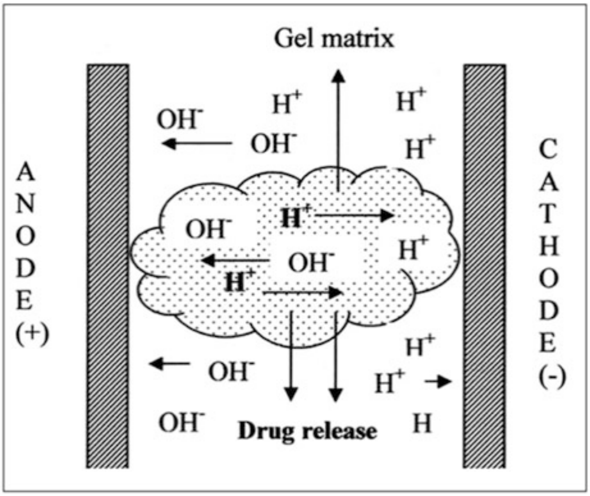

**Fig. 15.7** Mechanism of drug release in electrically sensitive hydrogels (Kulkarni and Biswanath 2007)

hydrogels. The necessary amount of the drug on-demand is released from transdermal systems and implants by electrically sensitive hydrogels (Juliano 1991). The mechanism of drug release from electric-responsive hydrogel is shown in Fig. 15.7. The literature shows that, under the control of an electrical current, ionic substances can be transmitted via the skin and the rate of release based on the length and quantum of the electrical stimulus. Electrical stimulation is often used in feedback-driven systems to integrate sensors and microelectronics (Juliano 1991; Ma et al. 1995). As they comprise high concentrations of ionizable functional groups, the electrically sensitive hydrogels also display a response to pH (Scranton et al. 1995). There are polyanions, polycations, and an amphoteric polyelectrolyte in the polymers that are so far examined. Also researched were naturally occurring polymers like hyaluronic acid (HA), chondroitin sulfate, agarose, carbomer, xanthan gum, calcium alginates, and synthetic polymers such as acrylate and methacrylate derivatives such as partially hydrolyzed polyacrylamide and polyamide (amide dimethyl aminopropyl acryl).

An electro-responsive hydrogel, for instance, can react to oscillatory volumetric adjustments comparable to the deformation produced in cartilage (Sundelacruz et al. 2009; Xue et al. 2016). Complex multicomponent gels or interpenetrating polymer networks (IPNs) have been synthesized to improve the electrical stimuli (Yuk et al. 1992). Calcium alginate/poly(acrylic acid) specimens were fabricated by Yuk et al. (1992), where the poly(acrylic acid) chains were embedded through the matrix of calcium alginate. The poly(acrylic acid) includes a huge number of free carboxylic groups and thus demonstrates the responsiveness to electrical stimulation and pH. The findings show that increasing the ratio of poly(acrylic acid) in the system improves the sensitivity to pH and electrical signals (Kulkarni and Biswanath 2007). The IPNs of polyvinyl alcohol and poly(acrylic acid) have also shown a similar increase in electrical sensitivity by increasing the quantity of free ionizable groups in hydrogels (Kim and Lee 1999). Kwon et al. proposed a complex type of electrically sensitive hydrogel, in which the cationic polyallylamine solution was combined with anionic heparin solution to form a complex by ionic bonding between the positively charged polyallylamine $NH^{3+}$ groups and the heparin $COO^-$ and $SO^{3+}$ groups (Kwon et al. 1991, 1994). The deionization of the carboxyl, sulfate, and amine groups demonstrated dissociation of the gel complex and gel erosion at $pH < 2$ and $pH > 11$ (Kwon et al. 1994).

Many hydrogels cross-linked by decreased graphene oxide or triblock copolymer micelles are being recently designed and shown exemplary electro-response and mechanical properties Liu et al. (2016a, b). Several hydrogels reinforced by decreased graphene oxide or triblock copolymer micelles are being recently designed who have shown exemplary electro-response and mechanical properties Liu et al. (2016a, b). For electro-responsive hydrogels for use as flexible fluid micro-actuators, direction-specific distribution components, and smart switches, the controllable bending direction is necessary (Choi et al. 1994; Yang et al. 2017). For example, based on the control of cross-linking density, an electro-responsive hydrogel with bidirectional bending behavior was established and the conceptual design was inspired by theoretical modeling of osmotic pressure changes (Lim et al. 2011).

### Nanoreinforced Hydrogels

Hydrogels were an appropriate candidate for tissue engineering of the several available commercially scaffolding biomaterials since they provide a biomimetic and hydrated 3D microenvironment to help cellular functions (Annabi et al. 2014; Peppas et al. 2006; Ravi et al. 2015). In simplistic words, such gels are mainly composed of water (usually around 90%) and their channel building blocks can be diverse (Benoit et al. 2008; Chaudhuri et al. 2016; Peppas et al. 2006). Importantly, hydrogels offer a complex and often permissive microenvironment that supports native-like extracellular matrix (ECM) features such including anchorage, signaling, nutrient transport, structural integrity, and homeostasis (Annabi et al. 2016; Peppas et al. 2006). Besides, these techniques can lead to unwanted restrictions on hydrogel's mechanical strength and electrical conductivity. Nanomaterials are quickly evolving throughout this aspect as a successful one-step method to attenuate the characteristics of hydrogels despite sacrificing the exchange of nutrients with the surrounding environment (Shin et al. 2012, 2013). However, most of the nanomaterials examined to date had influenced the mechanical properties of hydrogels, and significantly, a few of these materials also display inherent electrical properties and biological activity (e.g., cell biding motifs) that are instrumental in organ regeneration (Dvir et al. 2011; Xavier et al. 2015). Furthermore, the introduction of nanomaterial into cell-laden hydrogels offers a smart approach for the development of multipurpose tissue constructs that blend perfectly into the human body. Of all the many multipurpose biomaterials currently ongoing, nanoreinforced hydrogels are by far the most easily adapted in a clinical environment (Ramon-Azcon et al. 2013). This versatility stems partly from the ability to be able to develop synthetic nanomaterials to execute a multitude of tasks that would now have to be conducted inside a hydrogel by different components (i.e., normal, synthetic, and biological). To date, to improve the framework of hydrogels, some nanostructures, broadly categorized either as mineral-based or conductive nanomaterials, have been synthesized. Mineral-based nanomaterials comprise numerous clay-based platelets (Xavier et al. 2015) and ceramic nanoparticles, whereas conductive nanomaterials, namely carbon nanotubes (CNTs) and graphene are generally carbon-based (Annabi et al. 2016; Memic et al. 2015; Shin et al. 2012, 2015). Almost all of these devices still have not achieved their great opportunity to generate off-the-shelf-engineered organs and tissues, though much improvement has been achieved in engineering their related nanocomposite hydrogels. We expect that along with the addition of a new group of biomaterials wherein living tissues are fused with inanimate nanomaterials, the so-called "cyborganic tissues" of science fiction folklore, enhanced comprehension of their tissue engineering efficiency would drive significant breakthroughs in tissue engineering (Mehrali et al. 2017).

### Hemicellulose-Reinforced Nanocellulose Hydrogels

Polysaccharides are finding a growing range of additional uses as pharmaceutical and biotechnology products, e.g., as biocompatible hydrogels or scaffolds in tissue engineering, as artificial skin for the healing process, and as a biodegradable drug delivery carrier because of their non-toxicity, biocompatibility, biodegradability, and in certain cases, unique therapeutic activities (Liu et al. 2015; Popa 2011; Šimkovic 2013). Use of such biocomposites to build a provisional wound management device on the injury surfaces or to replace diseased or damaged tissues in the context of three-dimensional (3D) matrices has led to advanced wound care and tissue engineering (Czaja et al. 2007; Moroni et al. 2006). The challenge was to find appropriate composite matrices which can serve as cell carriers, and also providers of the support structure and biochemical signals for tissue growth and regeneration, and it can facilitate the healing process and produce biologically organized and functional organs and tissues.

Because of their structural similarity with extracellular matrix (ECM) and because of their ability to maintain a humid environment, that is important for the healing process, hydrogels are favored as scaffolds for biomedical applications (Lin et al. 2011; Rimmer 2011). Recently, nanocellulose hydrogels particularly nanofibrillated cellulose (NFC) often referred to as cellulose nanofibrils (CNF) have been studied for possible application in the healing process. The NFC was seen to be non-cytotoxic (Alexandrescu et al. 2013; Chinga-Carrasco and Syverud 2014), to inhibit the production of common wound bacteria (Powell et al. 2016), to minimize inflammation, and improve the tissue repair process (Mertaniemi et al. 2016), to facilitate the adhesion, survival, proliferation, and gene expression of wound healing related fibroblast cells (Alexandrescu et al. 2013; Hua et al. 2014; Pereira et al. 2013), that are all fit for wound management applications (Bhattacharya et al. 2012). By regulating the hydrogel swelling capability (Liu et al. 2014, 2016a, b), or by adding biocompatible reinforcing agents like hemicelluloses, environmental strategies to tuning the mechanical characteristics of NFC hydrogel scaffolds for possible tissue engineering applications were documented (Bonilla et al. 2016). Hemicelluloses have multiple beneficial biological functions from numerous sources, such as antioxidant, antitumor, and immunomodulating function, and have been designed for tissue engineering, drug delivery, wound treatment, cancer prevention, diagnosis, and therapy applications (Liu et al. 2015).

#### 15.6.1.2 Films

The development of hemicellulose acetate films was recorded by Smart and Whistler as soon as 1949. In the food and medical supplies industry, films, and coatings made from recycled materials have various potential uses, like active food packaging, wound dressings, and medication capsules. To ensure flexibility, the need for a plasticizer is always required, and sorbitol, glycerol, and xylitol are by far the most widely used for hemicellulose films. Hemicelluloses are hydrophilic and films made from these materials are typically hygroscopic, leading to poor properties in high humidity environments. Chemical alteration of the polymer perhaps by bulk or surface modification is a way of overcoming these issues, as recently stated in review articles. Hemicellulose, like cellulose, is an excellent candidate for chemical modification and has a surplus of free hydroxyl groups scattered along its backbone and side chains. Characteristics such as crystallinity, solubility, and hydrophilicity can be changed by creating hemicellulose derivatives by functionalizing accessible hydroxyl groups. Utilizing strategies like esterification, etherification, or grafting processes, studies have described these possibilities. For instance, in conditions similar to cellulose, hemicellulose acetylation can be achieved with an exponential rise in hydrophobicity. To increase biological function, sulfation was used. Etherification reactions are being studied, like carboxymethylation, alkylation, and benzylation, although different mechanisms have added cationic moieties. As initiator sites, the free hydroxyl groups in hemicellulose were used to conduct polymerizations of a variety of monomers to form grafts (Hansen and Plackett 2008).

Built on petroleum materials, the benefits of being biodegradable in the atmosphere and excellent biocompatibility are shared by hemicellulose from sustainable biomass resources and can thus be utilized either as food packaging or as an edible film. Hemicellulose has a relatively low molecular weight, and hence a low strength, comparable with cellulose. Even so, due to its functional hydroxyl group and diverse structures, hemicellulose has specific benefits that are simple to change to satisfy different requirements. Biomass film substrates widely used include flat film and hollow film. In particular, hemicellulose is used in the form of a flat film, typically prepared by combining flow casting, casting, and drying film-forming solution onto a mold. In Fig. 15.8, the widely used preparation process is shown (Yuelong Zhao et al. 2020).

With the degradation of the environmental climate, to manufacture chemicals and products, it is important to substitute petroleum-based products with environmentally friendly lignocellulosic biomass comprising of cellulose, hemicellulose, and lignin (Cherubini 2010; Putro et al. 2016). The high hydrophilicity, moreover, renders hemicellulose film brittle underneath humid conditions, leading to poor mechanical properties while mixing with hydrophobic polymers owing to phase separation. Such limitations restrict the use of hemicellulose in high-value-added industries (Farhat et al. 2017). Several attempts have been made to increase hemicellulose hydrophobicity by chemical treatment, i.e., esterification, acetylation,

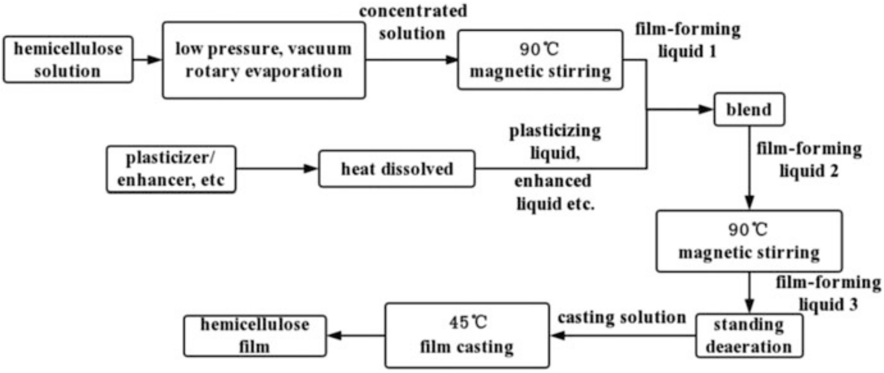

**Fig. 15.8** Flowchart of hemicellulose film preparation (Zhao et al. 2020)

etherification, fluorination, and cross-linking (Shao et al. 2019). Hemicellulose esterification applies to the reaction between hydroxyl groups. It is also possible to dissolve esterified hemicellulose in organic solvents gradually (Belmokaddem et al. 2011). CA is an effective and safe food additive, unlike conventional esterifying agents such as acetic acid and butyl chloride that can interact with hemicellulose under mild conditions and, meanwhile, form a cross-linked structure. While using CA to boost the mechanical properties, Wang and coworkers carried out the esterification of poly (vinyl alcohol) (PVA)/xylan composite films. The reaction pathway and the effect of CA content on hydrophobicity and oxygen permeability are not yet examined (Shao et al. 2019). In the abovementioned examination, several other hemicelluloses, PVA or other polymer works of literature, i.e., carboxyl methylcellulose or chitosan, are also applied as co-matrix to boost the formability of the film (Shao et al. 2019). To almost the same end, persistent and self-supporting hemicellulose films are often applied to plasticizers like glycerol, sorbitol, and xylitol. Throughout this study, via the process of alkaline hydrolysis preceded by alcohol precipitation, hemicellulose was extracted from poplar powder. To boost the film-forming capacity of hemicellulose, sorbitol and PVA were added. A range of hydrophobically modified hemicellulose films was then acquired by the solvent casting employing an esterification/cross-linking reaction by adding citric acid. By adjusting the CA content, the characteristics (thermal, mechanical, barrier, wettability) of the film were examined and updated. For the esterification/cross-linking reaction, a technique is implemented to illustrate the CA content dependency of film results. This study helps to understand the alteration and thus to better apply sustainable film as an alternative packaging with excellent barrier efficiency (Shao et al. 2019).

The characteristics of good film dressings are easy preparation process, exemplary moisture vapor transmission rate (WVTR), clarity, and cost-effectiveness (Dhivya et al. 2015; Kamoun et al. 2017). For producing film dressings, various synthetic and natural polymers and blends of them would have been investigated. Promises were shown for this function among some of the natural polymers chitosan, gelatin, alginate, pectin, and cellulose (Alavi et al. 2019; Boateng et al. 2013; Olewnik-Kruszkowska et al. 2019; Pawar et al. 2013; Rezk et al. 2019; Rezvanian et al. 2016). Conversely, the key drawbacks related to natural polymer-based films are inadequate mechanical strength, stability, low exudate-absorbing capability, and trauma site adherence (Naseri-Nosar and Ziora 2018). In an attempt to face these drawbacks, there is a need to investigate other biopolymers for these kinds of purposes. Hemicelluloses extracted through plant materials are increasing in popularity for its use in drug delivery and tissue engineering, being exceptionally biocompatible, biodegradable, and cost-efficient (Massey et al. 2016; Peng et al. 2011). They are the second biomass on earth with the most abundance. Arabinoxylan (AX) from psyllium (Plantago ovate) seed husk, among the most researched hemicelluloses, offers great potential for preparations for the delivery of drugs (Akbar et al. 2012a, b; Amin et al. 2013; Bhatia and Ahuja 2015). This polymer has indeed been commonly defined in terms of its structure and composition over the last two decades (Akbar et al. 2012b; Erum et al. 2015; Iqbal et al. 2011; Saghir et al. 2008, 2009). It has better sensitivity, water-absorption capability, and excellent film-forming properties, making it an excellent contender for the delivery of dressings for antibiotics.

Commonly used plasticizers in polysaccharide-based films are polyols (e.g., glycerol, sorbitol, and polyethylene glycol) because of their resemblance in structure to the polysaccharides and their hygroscopic nature that allows them to attract and retain water in the system. Reports of blends of two pure hemicelluloses are relatively rare in the literature. In previous studies, hemicelluloses have been used to produce films and coatings. A study by Qi et al. (2015) showed that the increase in the ratio of quaternized hemicelluloses (QH)/carboxymethyl cellulose (CMC) made the blends structurally dense, resulting in a significant increase in tensile strength and decreased water vapor permeability (WVP). However, when excess QH was added, there was a decrease in the tensile strength of the films and increased WVP. The transparencies decreased with the QH/CMC ratio. Ruiz et al. (2013) reported that the incorporation of hemicelluloses extracted from wheat straw under certain proportions in blends of κ-carrageenan/locust bean gum with glycerol as plasticizer slightly increased the water vapor barrier properties, opacity, and thermal properties of the blend (Mendes et al. 2017).

#### 15.6.1.3 Nanocomposites

Peng et al. integrated cellulose nanofibers (CNFs) in xylan (XH) films in the existence of plasticizers, suggested an inexpensive and easy method to manufacture high-quality hemicellulose-based nanocomposite film (Peng et al. 2011). Morphological research indicates that the XH film surface and CNF-reinforced nanocomposite film were predominantly comprised of nodules with a diameter of 10–70 nm and that CNFs were incorporated in the XH matrix. The high aspect ratio and good associations between the CNF and the XH matrix resulted in improved film-forming and major tensile strength development. Guan et al. also used the freeze-thaw technique to build a novel hybrid hydrogel from hemicelluloses isolated from holocellulose, PVA, and chitin nanowhiskers from bamboo (Phyllostachys pubescens) (Guan et al. 2014). PVA served a hydrogel scaffold role, while hemicelluloses demonstrated a strong hydrophilic and hydrogen-bonding character as a cross-linker with chitin nanowhiskers. As the percentage of chitin nanowhiskers increased, the material characteristics of the hydrogels were significantly improved; these hydrogels were considered possible candidates for use in tissue engineering applications. Japan has patented laminated films composed of one layer of a thermoplastic film (polyester) and another of carbon nanotubes and hemicellulose (Ciolacu and Darie 2016).

#### 15.6.1.4 Microparticles

Recently, Urtiga et al. (2020) described xylan-based microparticles for controlled delivery of mesalamine. They used xylan extracted from corn cobs to produce mesalamine-loaded microparticles (XMP5-ASA) by cross-linking polymerization technique utilizing non-hazardous cross-linking agents. A comparative study of the in vitro drug release from XMP5-ASA and from gastro-resistant capsules filled with XMP5-ASA (XMPCAP5-ASA) or 5-ASA was also performed. The release studies showed that XMPCAP5-ASA allowed more efficient drug retention in the simulated gastric fluid and a prolonged drug release lasting up to 24 h. XMPCAP5-ASA retained approximately 48% of its drug content after 6 h on the drug release assay. Thus, the encapsulation of 5-ASA into xylan microparticles together with gastro-resistant capsules allowed a better release control of the drug during different simulated gastrointestinal medium. In order to obtain visual and morphological characterization of xylan-based microparticles, the SEM (Fig. 15.9a–d) analysis was performed, wherein it was possible to observe the microparticles spherical shape with the presence of residuals on their surface, which can be related to the cross-linking agent that remained after washing process (Urtiga et al. 2020).

### 15.6.2 Biomedical Applications

Polysaccharides are finding growing numbers of potential uses as components for biomedical and pharmaceutical products, e.g., as biocompatible hydrogels or scaffolds in tissue engineering, as artificial skin for wound healing, and as a biodegradable carrier for delivery of drugs owing to their non-toxicity, biocompatibility, biodegradability, and complex therapeutic activities (Liu et al. 2015; Šimkovic 2013; Spiridon and Popa 2008). The use of biocomposites to establish a provisional wound management device on injury sites or to replace diseased or damaged tissues in the manner of three-dimensional (3D) matrices has resulted in advanced wound care and tissue engineering (Czaja et al. 2007; Moroni et al. 2006). The task was to find optimized composite matrices which can serve as cell carriers and also as a mechanical support and biochemical indicators for tissue repair and maturation and which can facilitate the recovery process and produce tissues and organs with biological structures and functions (Balakrishnan and Banerjee 2011).

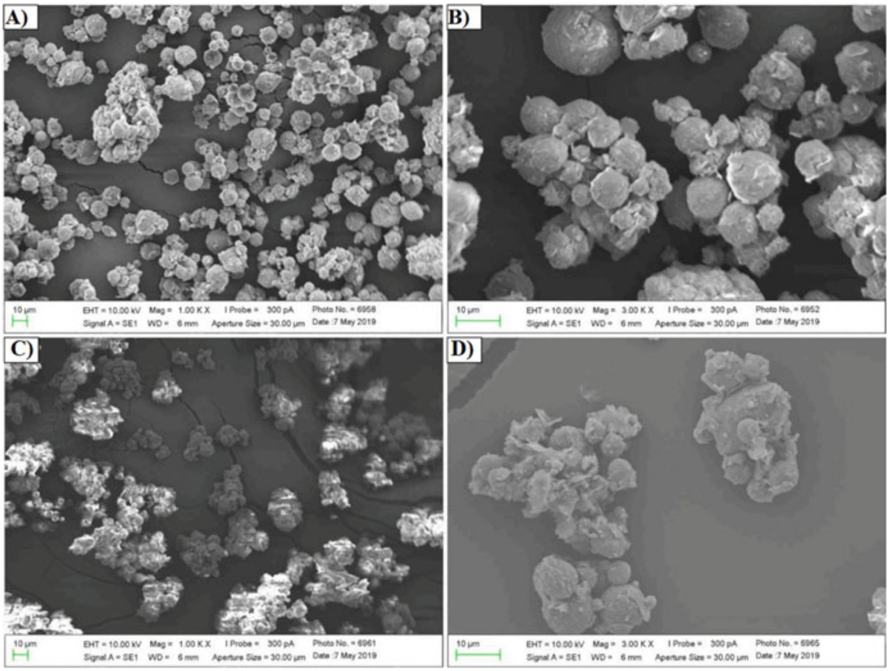

**Fig. 15.9** SEM images of xylan microparticles: XMP (**a**, **b**) and XMP5-ASA (**c**, **d**). (Reproduced from Urtiga et al. 2020 with kind permission of the copyright holder, Elsevier, Amsterdam)

#### 15.6.2.1 Wound Healing

A wound is a disturbance in the skin's anatomy and physiology which might be incurred by physical, chemical, or thermal damage, or pathology (Pawar et al. 2014; Simões et al. 2018). The wound healing phase commences immediately after the formation of the wound in an attempt to restore the disturbed skin function. This is a dynamic mechanism consisting of a series of orchestrated activities involving homeostasis, inflammation, proliferation, remodeling, and maturation of scars (Boateng et al. 2008; Huang et al. 2019a, b; Patel et al. 2018; Singh et al. 2013). Different aspects like diabetes mellitus, bacterial infection, inadequate wound treatment, and patient lifestyle could then exacerbate the wound healing process (Kirketerp-Møller et al. 2011; Phan et al. 2019). The host's immune response, as well as the injury recovery process, are disrupted in an infected wound that contains 106 CFU/mL of bacteria, that not only slows the tissue repair but can also have life-threatening implications (Bendy et al. 1964; Boateng et al. 2013; Ng and Leow 2015; Said et al. 2014). For this purpose, wound dressings are applied to the wound site to preserve the injury from bacterial infection, given antibiotics, absorb wound exudate as well as provide a moist atmosphere (required for ideal healing) (Alavi et al. 2019; Bowler et al. 2001; Simões et al. 2018). Nevertheless, in conjunction with topical antibiotic preparations, the use of traditional wound dressings (gauze, pads, and cotton) results in medication drainage, untidiness, and dryness of the injury site, resulting in poor tissue repair and patient acceptance. Therefore, a wound dressing must be established which can extend the antibiotics residence period in the infected wound, absorb exudate, and provide a moist condition across the injury area (Pawar et al. 2013).

Wound medicine presents a big obstacle to the worldwide medical system and creates a significant financial burden (Kamoun et al. 2017). Inevitably, skin repair for adults and overage individuals occurs; furthermore, wound healing is followed by bruising and the criteria cannot be fulfilled by conventional approaches. It was speculated that the dry and exposed wounds would heal more rapidly. When the first generation of wound dressings has introduced, this skepticism was reduced. The most widely traded dressings were dried wound dressings until the middle of 1970 (Vincent Edwards et al. 2001). Dried bandages keep the injured tissue dry due to the removal of exudates and fluids from the injury. These fluids leak out of the dressings, contributing to contamination of the wound. The dried dressings, as they bind to the wound surface and result in poor oxygen permeability, cause extreme pain during the removal period. Also, due to preserving the injury in dry conditions, they reduce the chance of epithelialization and cell proliferation. In 1970, humid wound dressing was adopted and demonstrated a quick recovery rate than dried dressings (Vincent Edwards et al. 2001). Furthermore, their wet environment enables it possible to keep the wound surface moist all the time, which increases the rate of epithelialization and cell growth. Hydrogels have been proven to be the dominant option for the implementation of wet wound dressings as they provide many benefits, such as holding the wound moist, permeating oxygen, removing wound exudates, shielding the injury from infection and contamination, and cleaning it quickly and comfortably (Kamoun et al. 2017).

Hydrogel dressings are marketed with different brands, like GRX wound gel, Biolex, TegaGel, NuGel, Carrasyn, 2nd Skin Fexderm, ExuDry dressing, and Cultinova gel (Kamoun et al. 2017). Polyvinyl alcohol (PVA) is already identified as being the most commonly considered hydrogel amongst these hydrogels used for wet dressings due to the superior performance of the PVA-based hydrogels relative to their counterparts. It is combined with certain natural polysaccharides or some synthetic ones to overcome the mechanical properties of the PVA problem (Kamoun et al. 2017). The skin's pH is slightly acidic and ranges from 4 to 6 (Schneider et al. 2007). Moreover, skin injuries introduce the skin to the internal body fluids which have physiological pH (7.4)—leading to an increase in the pH of the affected skin. The pH of wounds was attributed to differences in the scale of 6.5–8.5 based on wound situations. For wound healing, wound cells interact with a range of bioactive molecules: cytokines, extracellular matrix proteins, and growth factors (Banerjee et al. 2012). The association is directly or indirectly influenced by the pH of the wound (Werner and Grose 2003). Thus, pH-responsive hydrogels can play an important role in the reaction to cell growth and also control the wound status.

Banerjee et al. discussed a pH-responsive hydrogel which continued to release growth factors to speed up the healing of the wound (Banerjee et al. 2012). Through radical copolymerization, the pH-responsive hydrogel was composed of poly (*N*-isopropyl acrylamide-co-acrylic acid). The hydrogel was filled with bovine serum albumin (BSA), vascular endothelial growth factor, and epithermal growth factor, which were discharged inside the injury pH range (6.7–7.9) at varying rates for 14 days. With such an improvement in wound pH, releasing the growth factors was revolutionary. The loaded hydrogel with growth factors was evaluated on the murine excisional wound model and showed significant improvement in wound healing relative to traditional growth factor therapy with a continuous release (Mirani et al. 2017). The pH-hydrogel released antibiotic agents and used pH detection as an indicator to control bacterial infections of wound sites. The hydrogel precision was equivalent to commercial systems for the identification of bacterial infections and the smartphone was used as a reader for wound conditions (Hendi et al. 2020).

#### 15.6.2.2 Tissue Engineering

Tissue engineering advancements provide the ability to solve many medical concerns, varying from aging populations to cancer (Ratner and Bryant 2004). By combining biomaterials and cells, tissue engineers strive to repair or replace the lost functionality of injured tissue or collapsed organs. Some of their most major applications at the present are in organ regeneration (Khademhosseini et al. 2009) and disease modeling (Lowenthal and Gerecht 2016) and cyborganics as biological components (Giselbrecht et al. 2013). Earlier efforts have progressed in developing living tissues in three-dimensional (3D) scaffolds that provide the required stimuli for stem cells to trigger lineage-specific segregation into structures similar to tissue (Khademhosseini et al. 2009; Ravi et al. 2015; Santos et al. 2012). In reality, much of the existing scaffolds are rigid insulators, so they do not integrate well with the body's elastic, dynamic, and electroactive organs (Fleischer and Dvir 2013). They do not imitate the complex architecture of indigenous tissues, nor because they provide the mechanical, electrical, and biological stimuli required to orchestrate mature and functional tissue cells. In the efficient production of artificial and native-like tissues and organs, designing multipurpose and adaptive cellular microenvironments is therefore imperative. Nevertheless, in the field of tissue engineering, the prevailing lack of technique to build scaffolds that replicate the unique characteristics of human tissues is still a crucial bottleneck that must be tackled (Mehrali et al. 2017).

Research work on cartilage tissue engineering also depends on the use of hydrogels to transport chondrocytes and preserve their phenotype. A benefit of hydrogels is that they've been manufactured under mild conditions which are consistent with cell viability, like chondrocytes, and hydrogel properties are also developed to facilitate minimally invasive surgery implementations (Anseth et al. 2002; Betre et al. 2002; Bryant et al. 2004; Bryant and Anseth 2002, 2003; Elisseeff et al. 2001; Martens et al. 2003; Park et al. 2004; Stile et al. 1999). Utilizing embodied chondrocytes, several various forms of hydrogels have also been examined for the development of cartilage. Alginate was shown to cause redifferentiation by monolayer cell culture of chondrocytes which were dedifferentiated (Bidarra et al. 2014). For cartilage regeneration, certain hydrogels also have been investigated. Owing to its ability to also be rendered into lightly cross-linked hydrogels that can be inserted into the body via a needle, thermoresponsive polymers with low critical solution temperatures below 37 °C are particularly promising. They solidify and stay in place once they hit body temperature, assuming the form of the atmosphere to which they have been delivered.

Healy et al. synthesized hydrogels dependent on poly (*N*-isopropyl acrylamide) comprising peptide-based cross-links which are explicitly deteriorated mostly during wound healing reaction by metalloproteinases participating in the remodeling of the extracellular matrix (Stile et al. 1999, 2003). These hydrogels have been provided to effectively enhance the viability of bovine articular chondrocytes for at least 28 days in vitro. They could've been injected via a small needle and the thermoresponsive characteristics of the hydrogel materials could quickly stabilize them in situ. The extracellular matrix containing characteristics similar to natural cartilage has been formed by the chondrocytes encompassed in such thermoresponsive hydrogels. Sulfated polysaccharides were stained, there was confirmation that perhaps the material of the hydrogel allowed chondrocytes to proliferate inside those hydrogels (Stile et al. 1999). For minimal invasive applications, therefore, thermoresponsive hydrogels show great promise.

In hard tissue applications, hydrogels also have been introduced. Their feasibility to be produced in situ during mild reaction conditions that are consistent with both the durability of biomolecules and cells has rendered them ideal materials for the treatment of bone defects and speeding healing in orthopedic applications (Gibbs et al. 2016). For bone healing applications, various hydrogel systems have been investigated. Some systems incorporate over than one portion of hydrogel and often involve an extracellular matrix element like hyaluronic acid (Jung et al. 2018) or the incorporation of sequences of RGD peptides that enable cell adhesion (Coletta et al. 2017; Gibbs et al. 2016).

The possibility that hydrogels can be compatible with cell viability, can maintain protein and other biomolecules biological function, and could even be injected or polymerized in situ in mild conditions, makes them essential materials for stem cell therapy (Bayer et al. 2017; Betre et al. 2002; Coletta et al. 2017; Jung et al. 2018; Metzger et al. 2015). Stem cell therapy suggests that their distinction depends on a variety of environmental cues, whereby the matrix's stiffness plays a significant role (Lv et al. 2015). The mechanical properties of hydrogels (hence their rigidity) are hugely reliant on their extent of cross-linking. For such a purpose, numerous studies have shown that the mechanical properties of hydrogels, which can be regulated by the degree of cross-linking, could influence stem cell differentiation (Alakpa et al. 2016; Banerjee et al. 2009; Goldshmid and Seliktar 2017; Lanniel et al. 2011). Injectable stem cell-containing hydrogels are being tested for cardiac tissue repair (Hasan et al. 2015; Zhu and Marchant 2011). Injectable PEG-based hydrogels, or fibrinogen-conjugated Tetronic®, are also used to boost heart function by conjugating the left decreasing coronary artery after triggering infarctions in a rodent model. The results revealed that higher heart function regeneration and neovascularization were provided by the highest modulus hydrogels. This demonstrated that hydrogels alone have a protective effect mostly on the treatment of post-infarction myocardial injury by preventing damaging tissue remodeling after a heart attack (Plotkin et al. 2014). It will also be reasonable to believe that incorporated stem cells would contribute to the regeneration of the damaged myocardium after an infarction (Ryu et al. 2005) (Table 15.2).

**Table 15.2** Hemicellulose-based drug delivery systems

| Formulation | Composition | Drug used | Application | Therapeutic outcome | References |
|---|---|---|---|---|---|
| Hydrogels | | | | | |
| Temperature-sensitive hydrogel | Hemicellulose obtained from acetic acid pulping of eucalyptus and *N*-isopropyl acrylamide | – | – | Showed potential as smart materials for medical applications. | Yang et al. (2011) |
| pH-sensitive hydrogel | Hemicellulose from wheat straw | Acetylsalicylic acid and theophylline | – | Hemicellulose-based hydrogels can be used in biomedical fields, especially for controlled drug release | Sun et al. (2013) |
| pH-responsive hydrogel | Chitosan | Theophylline | Nocturnal asthma | Extended release of theophylline in the intestine | Kumar Singh Yadav and Shivakumar (2012) |
| Magnetic field responsive hydrogel | Polyacrylamide | Vitamin B2 | Vitamin supplement | It showed a relatively slower release in the presence of an applied magnetics field. | Namdeo et al. (2009) |
| Nanoreinforced hydrogels | Hemicelluloses, polyvinyl alcohol, and chitin nanowhiskers | – | Tissue engineering | Prepared hydrogel shows promise for tissue engineering applications | Guan et al. (2014) |
| Hemicellulose-reinforced nanocellulose hydrogels | Nanofibrillated cellulose (NFC) with hemicellulose (galactogluco mannan (GGM), xyloglucan (XG), and xylan) | – | Wound healing | Promising scaffolds in wound healing and promoting cell adhesion, growth, and proliferation. | Liu et al. (2016a, b) |
| Films | | | | | |
| Hemicellulose-based films for antibacterial wound-dressing application | Arabinoxylan | Gentamicin | Wound dressing | Hemicellulose-based films are promising materials for the dressing of infected wounds. | Ahmad et al. (2020) |

(continued)

**Table 15.2** (continued)

| Formulation | Composition | Drug used | Application | Therapeutic outcome | References |
|---|---|---|---|---|---|
| Nano composites | | | | | |
| Nano composite film | Wood auto-hydrolysates (WH) combined with montmorillonite (MMT) and graphene oxide (GO) | – | – | It can used for fabrication of fire-protective films, coatings, packaging, etc. | Chen et al. (2018) |
| Wound healing | | | | | |
| Hemicellulose-based films for antibacterial wound-dressing Hemicellulose-based films for antibacterial wound dressing | Hemicellulose (arabinoxylan) isolated from psyllium husk | Gentamicin | Wound healing | It is a promising material for the dressing of infected wounds. | Ahmad et al. (2020) |
| Tissue engineering | | | | | |
| Xylan hemicellulose improves chitosan hydrogel | Hemicellulose xylan with chitosan | – | Bone tissue regeneration | It is a bone graft substitute able to aid in the repair of large bone defects | Bush et al. (2016) |

## 15.7 Conclusion and Future Perspectives

The amount of hemicellulose studies covered by this study suggests that the significance of all hemicellulose forms as active constituents and isolated polymers throughout the last many years has increased significantly. In addition to recognized hemicelluloses, consideration has been devoted to the primary structure, physicochemical, physical, and different functional properties of hemicelluloses originating from various sources, with a significant emphasis on biomedical applications. The utility, in an industrial and biomedical sense, of hemicellulose-based or derived materials, is already beyond doubt. This will encourage additional progress in the development of natural-source isolation and purification approaches and the advancement of analytical instruments to structurally classify isolated hemicelluloses and their derivatives. Polysaccharides exhibit diversity and versatility, linked to their complex structures, not seen in many other groups of polymers, as figured out during this study. A really wide variety of applications facilitates this particularity, and derivatizations further expand their potential uses. This review of polysaccharide hydrogels in use for delivery of drugs and strongly linked implementations clearly shows how a growing number of researchers from all over the world are involved in the fabrication and characterization of various new kinds of hydrogels with remarkable features that make them ideal for a wide range of developments in the areas.

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